

Error-Correcting Codes for Nanopore Sequencing

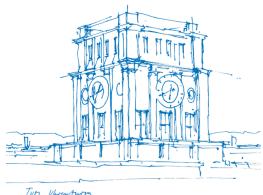
Anisha Banerjee¹

Joint work with

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¹Technical University of Munich Institute for Communications Engineering

²Technion – Israel Institute of Technology Department of Computer Science



June 26, 2023

Outline

Introduction

Channel Model

Minimum Redundancy

Error-correcting Code

Conclusion

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Channel Mode

Minimum Redundancy

Error-correcting Code

Conclusion

Solver 100, 201



- Need for dense, reliable, robust storage media
 - ► Molecular storage paradigms e.g., DNA storage.¹

¹R. Heckel et al., "A characterization of the DNA data storage channel," Scientific Reports, vol. 9, no. 9663, Jul. 2019.

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- Faster, cheaper sequencers in development.

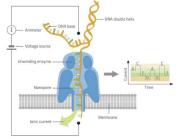
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- Need for dense, reliable, robust storage media
 - ► Molecular storage paradigms e.g., DNA storage.¹
- Faster, cheaper sequencers in development.
- Nanopore sequencing²:
 - + Can read longer DNA strands
 - + More portable
 - + Low cost
 - High error rates







Source: "Decoding DNA with a pocket-sized sequencer." Science in School. https://www.scienceinschool.org/article/2018/decoding-dna-pocket-sized-sequencer/

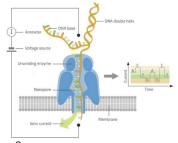
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 - High error rates
- Aim: Design coding techniques tailored for nanopore sequencing!







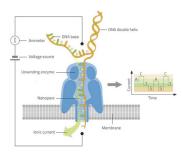
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Nanopore Sequencing





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- Sources of noise [MDK18] :
 - ▶ Nanopore holds $\ell > 1$ nucleotides at a time \rightarrow Intersymbol interference (ISI)!
 - \blacktriangleright Strand moves irregularly \rightarrow backtracking & skipping.
 - Noisy measurements

[[]MDK18] W. Mao et al., "Models and information-theoretic bounds for nanopore sequencing," *IEEE Trans. Inf. Theory*, vol. 64, no. 4, pp. 3216–3236, Apr. 2018

Prior Work



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- [MDK18] → Introduced a mathematical model.
 - \rightarrow Established bounds on capacity.
- ullet [HCW21] ullet Algorithm to compute capacity of an abstracted, deterministic channel model.
 - → Coding schemes.
- [MVS22] → Finite-state Markov channel model incorporating major noise sources.
 - → Generalized MAP detection algorithms.
- [CVVY21] considered a similar channel for racetrack memories:
 - → Computed information limits.
 - → Proposed error-correcting codes.

[MDK18] W. Mao et al., "Models and information-theoretic bounds for nanopore sequencing," *IEEE Trans. Inf. Theory*, vol. 64, no. 4, pp. 3216–3236, Apr. 2018

[HCW21] R. Hulett *et al.*, "On Coding for an Abstracted Nanopore Channel for DNA Storage," in *IEEE Intl. Symp. on Inf. Theory (ISIT)*, Melbourne, Australia, Jul. 2021, pp. 2465–2470

[MVS22] B. McBain *et al.*, "Finite-state semi-markov channels for nanopore sequencing," in *IEEE Intl. Symp. Inf. Theory (ISIT)*, Espoo, Finland, Jun. 2022, pp. 216–221

[CVVY21] Y. M. Chee *et al.*, "Coding for transverse-reads in domain wall memories," in *IEEE Intl. Symp. Inf. Theory (ISIT)*, Melbourne, Australia, Jul. 2021, pp. 2924–2929

Introduction

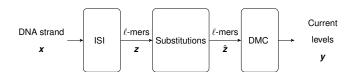
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Error-correcting Code

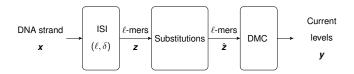
Conclusion





W. Mao et al., "Models and information-theoretic bounds for nanopore sequencing," IEEE Trans. Inf. Theory, vol. 64, no. 4, pp. 3216–3236, Apr. 2018



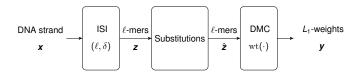


We model

- ISI as (ℓ, δ) -sliding window
- Measurement noise as substitutions

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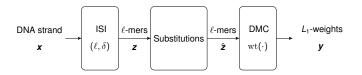
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Assumptions:

- Input $\mathbf{x} \in \{0, 1\}^n$
- Output: L_1 -weights of ℓ -mers

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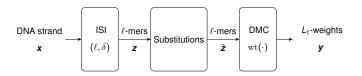
- Input $\mathbf{x} \in \{0, 1\}^n$
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Example ($\ell = 3, \delta = 1$)

$$(1, 0, 1, 1, 0, 0) = \mathbf{x} \longrightarrow \underbrace{\begin{pmatrix} (\ell, \delta) \\ \text{windowing} \end{pmatrix}} \quad \underbrace{\ell\text{-mers}} \quad \text{wt}(\cdot)$$

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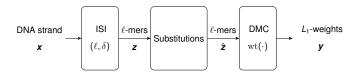
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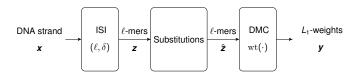
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Example (
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$$(1,0,1,1,0,0) = x \longrightarrow \underbrace{\begin{pmatrix} (\ell,\delta) \\ \text{windowing} \end{pmatrix}} \quad \ell\text{-mers} \longrightarrow \underbrace{\text{wt}(\cdot)} \quad (1,1),$$

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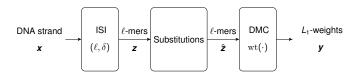
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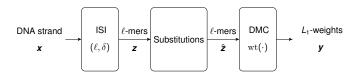
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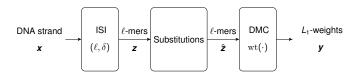
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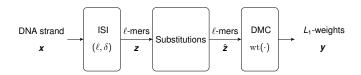
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Example (
$$\ell = 3$$
, $\delta = 1$)

$$(1\ ,\ 0\ ,\ 1\ , \textcolor{red}{\textcolor{red}{\color{blue}1}}, \textcolor{red}{\color{blue}0}, \textcolor{red}{\color{blue}0}) = \textbf{\textit{x}} \longrightarrow (\ell, \delta) \qquad \qquad \text{ℓ-mers} \qquad \text{$\operatorname{wt}(\cdot)$} \longrightarrow (1\ ,\ 1\ ,\ 2\ ,\ 2\ ,\ 2\ , \textcolor{red}{\textcolor{blue}1}, \textcolor{blue}{\color{blue}1}, \textcolor{blue}{\color{blue}1}, \textcolor{blue}{\color{blue}1}, \textcolor{blue}{\color{blue}1}, \textcolor{blue}{\color{blue}1}, \textcolor{blue}{\color{blue}2}, \textcolor{blue}2, \textcolor{blue}2,$$





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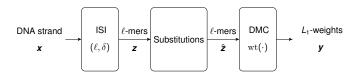
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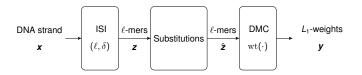
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W. Mao et al., "Models and information-theoretic bounds for nanopore sequencing," IEEE Trans. Inf. Theory, vol. 64, no. 4, pp. 3216–3236, Apr. 2018





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Definition

The (ℓ, δ) -read vector of any $\mathbf{x} \in \Sigma_2^n$ is

$$\mathcal{R}_{\ell,\delta}(\boldsymbol{x}) = (\operatorname{wt}(\boldsymbol{x}_{\delta-\ell+1}^{\delta}), \operatorname{wt}(\boldsymbol{x}_{2\delta-\ell+1}^{2\delta}), \dots, \operatorname{wt}(\boldsymbol{x}_{n-\delta+1}^{n+\ell-\delta})),$$

where for $i \notin [n]$, let $x_i = 0$ and $wt(\cdot)$ denotes L_1 -weight.

Y. M. Chee *et al.*, "Coding for transverse-reads in domain wall memories," in *IEEE Intl. Symp. Inf. Theory (ISIT)*, Melbourne, Australia, Jul. 2021, pp. 2924–2929



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where for $i \notin [n]$, let $x_i = 0$ and $wt(\cdot)$ denotes L_1 -weight.

Our Results

- $\log \log n o(1)$ min redundancy to correct 1 substitution in $(\ell \ge 3, \delta = 1)$ -read vectors
- Introduce a 1-substitution correcting code that is optimal up to a constant.

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Definition

The (ℓ, δ) -read vector of any $\mathbf{x} \in \Sigma_2^n$ is of length $(n + \ell)/\delta - 1$ and denoted by

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• We limit focus to $\ell \geq$ 3, $\delta =$ 1.



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- We limit focus to $\ell \geq$ 3, $\delta =$ 1.
- Read vectors have special properties.

$$\blacktriangleright |\mathcal{R}(\boldsymbol{x})_i - \mathcal{R}(\boldsymbol{x})_{i-1}| \leq 1 \iff \mathcal{R}(\boldsymbol{x})_i - \mathcal{R}(\boldsymbol{x})_{i-1} = x_i - x_{i-\ell}$$



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- Can correct errors of abs. value ≥ 2.



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- $ightharpoonup \sum_{i} \mathcal{R}(\mathbf{x})_{i} \bmod \ell = 0$, etc.
- Can correct errors of abs. value ≥ 2.
 - ► Suffices to consider ±1 errors.



Definition

C is a t-substitution $(\ell, 1)$ -read code if for all $\mathbf{x}, \mathbf{y} \in C$,

$$d_H(\mathcal{R}(\boldsymbol{x}), \mathcal{R}(\boldsymbol{y})) > 2t,$$

where $d_H(\cdot, \cdot)$ denotes Hamming distance.



Definition

 \mathcal{C} is a *t*-substitution (ℓ , 1)-read code if for all \mathbf{x} , $\mathbf{y} \in \mathcal{C}$,

$$d_H(\mathcal{R}(\boldsymbol{x}), \mathcal{R}(\boldsymbol{y})) > 2t,$$

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• Aim: Find a 1-substitution $(\ell, 1)$ -read code.



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 - ► Minimum redundancy required?



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- Aim: Find a 1-substitution (ℓ , 1)-read code.
 - ► Minimum redundancy required?
 - ▶ When does $d_H(\mathcal{R}(\mathbf{x}), \mathcal{R}(\mathbf{y})) \leq 2$ occur?

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• When does $d_H(\mathcal{R}(\mathbf{x}), \mathcal{R}(\mathbf{y})) \leq 2$ occur?

Lemma

For $\ell > 1$, $\delta = 1$ and any distinct $\textbf{\textit{x}}, \textbf{\textit{y}} \in \{0,1\}^n$, $d_H(\mathcal{R}(\textbf{\textit{x}}), \mathcal{R}(\textbf{\textit{y}})) \neq 1$.



• When does $d_H(\mathcal{R}(\mathbf{x}), \mathcal{R}(\mathbf{y})) \leq 2$ occur?

Lemma

For $\ell > 1$, $\delta = 1$ and any distinct $\textbf{\textit{x}}, \textbf{\textit{y}} \in \{0,1\}^n$, $d_H(\mathcal{R}(\textbf{\textit{x}}), \mathcal{R}(\textbf{\textit{y}})) \neq 1$.

Proof idea:

- Use read-vector properties:
 - $ightharpoonup \sum_i \mathcal{R}_i \bmod \ell = 0.$
 - $\blacktriangleright |\mathcal{R}_{i+1} \mathcal{R}_i| \leq 1.$

• When does $d_H(\mathcal{R}(\mathbf{x}), \mathcal{R}(\mathbf{y})) = 2$ occur?



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Theorem

For $\ell \geq 3$ and any $\boldsymbol{x}, \boldsymbol{y} \in \Sigma_2^n$, the following are equivalent:

1.
$$d_H(\mathcal{R}(\mathbf{x}), \mathcal{R}(\mathbf{y})) = 2$$
.

$$\mathbf{x} = (1,0,1,1,0,0), \ \mathcal{R}(\mathbf{x}) = (1,1,2,2,2,1,0,0)$$

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For $\ell \geq 3$ and any $\boldsymbol{x}, \boldsymbol{y} \in \Sigma_2^n$, the following are equivalent:

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- 3. There exist $p \ge 1$, $i \in [n (p 1)\ell 1]$ s.t. $\forall m \in \Sigma_p$, $\mathbf{x}_{i+m\ell}^{i+m\ell+1} = (1,0)$, $\mathbf{y}_{i+m\ell}^{i+m\ell+1} = (0,1)$ (or vice versa), and $x_r = y_r$ for all $r \notin \bigcup_{m \in \Sigma_n} \{i + m\ell, i + m\ell + 1\}$.

Further, if these conditions hold, then $j = i + p\ell$ in the above notation.

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• Consider graph with all vertices in $\{0,1\}^n$.

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[[]K94] D. E. Knuth, "The sandwich theorem," The Electronic Journal of Combinatorics, vol. 1, no. 1, A1, Apr. 1994 [CKY22] J. Chrisnata et al., "Correcting deletions with multiple reads," IEEE Trans. Inf. Theory, vol. 68, no. 11, pp. 7141–7158, Nov. 2022

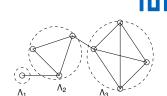
ТИП

- Consider graph with all vertices in $\{0,1\}^n$.
 - ▶ $x, y \in \{0, 1\}^n$ adjacent iff $d_H(\mathcal{R}(x), \mathcal{R}(y)) = 2$.



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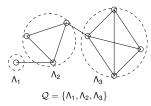
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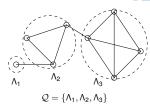
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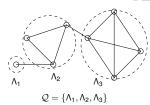
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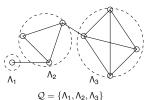
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Theorem

The redundancy of a 1-substitution $(\ell, 1)$ -read code is bounded from below by

$$\log_2\log_2(n)-o(1).$$

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Introduction

Channel Mode

Minimum Redundancy

Error-correcting Code

Conclusion



$$\mathcal{R}(\boldsymbol{x}) = \left(\operatorname{wt}(\boldsymbol{x}_1), \operatorname{wt}(\boldsymbol{x}_1^2), \ldots \operatorname{wt}(\boldsymbol{x}_1^\ell), \operatorname{wt}(\boldsymbol{x}_2^{\ell+1}), \ldots \ldots \operatorname{wt}(\boldsymbol{x}_{n-\ell+1}^n), \ldots, \operatorname{wt}(\boldsymbol{x}_{n-1}^n), \operatorname{wt}(\boldsymbol{x}_n)\right)$$



$$\left(0,\operatorname{wt}(\textbf{\textit{x}}_1),\operatorname{wt}(\textbf{\textit{x}}_1^2),\ldots\operatorname{wt}(\textbf{\textit{x}}_1^\ell),\operatorname{wt}(\textbf{\textit{x}}_2^{\ell+1}),\ldots\ldots\operatorname{wt}(\textbf{\textit{x}}_{n-\ell+1}^n),\ldots,\operatorname{wt}(\textbf{\textit{x}}_{n-1}^n),\operatorname{wt}(\textbf{\textit{x}}_n),0\right)$$



$$\begin{aligned} \big(0, \operatorname{wt}(x_1), \operatorname{wt}(\boldsymbol{x}_1^2), \dots \operatorname{wt}(\boldsymbol{x}_1^\ell), \operatorname{wt}(\boldsymbol{x}_2^{\ell+1}), \dots \dots \operatorname{wt}(\boldsymbol{x}_{n-\ell+1}^n), \dots, \operatorname{wt}(\boldsymbol{x}_{n-1}^n), \operatorname{wt}(x_n), 0 \big) \\ & \qquad \qquad \Big| \text{ Derivative } \\ & \qquad \qquad \big(x_1, x_2, \dots, x_\ell, x_{\ell+1} - x_1, x_{\ell+2} - x_2, \dots, x_n - x_{n-\ell}, -x_{n-\ell+1}, \dots, -x_{n-1}, -x_n \big) \end{aligned}$$



$$(0, \operatorname{wt}(x_1), \operatorname{wt}(\boldsymbol{x}_1^2), \dots \operatorname{wt}(\boldsymbol{x}_1^\ell), \operatorname{wt}(\boldsymbol{x}_2^{\ell+1}), \dots \dots \operatorname{wt}(\boldsymbol{x}_{n-\ell+1}^n), \dots, \operatorname{wt}(\boldsymbol{x}_{n-1}^n), \operatorname{wt}(x_n), 0)$$

$$\qquad \qquad \qquad \Big| \text{ Derivative }$$

$$(x_1, x_2, \dots, x_\ell, x_{\ell+1} - x_1, x_{\ell+2} - x_2, \dots, x_n - x_{n-\ell}, -x_{n-\ell+1}, \dots, -x_{n-1}, -x_n)$$

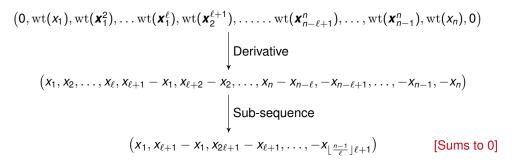
$$\qquad \qquad \qquad \Big| \text{ Sub-sequence }$$

$$(x_1, x_{\ell+1} - x_1, x_{2\ell+1} - x_{\ell+1}, \dots, -x_{\lfloor \frac{n-1}{\ell} \rfloor \ell+1})$$



• Call this **read sub-derivative** $\Delta^0(\mathbf{x})$.





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- Call this read sub-derivative $\Delta^{\alpha}(\mathbf{x})$, $\alpha \in \{0, \dots, \ell-1\}$.
- Helps reconstruct subsequence $(x_{\alpha+1}, x_{\ell+\alpha+1}, x_{2\ell+\alpha+1}, \ldots)$.

Read Sub-derivative



Sub-derivative of read vector

For any $\alpha \in \{0, \dots, \ell-1\}$, the α -th read sub-derivative of $\mathcal{R}(\boldsymbol{x})$ is

$$\begin{split} \Delta^{\alpha}(\mathbf{x}) = & (\mathcal{R}(\mathbf{x})_{\alpha+1} - \mathcal{R}(\mathbf{x})_{\alpha}, \mathcal{R}(\mathbf{x})_{\alpha+\ell+1} - \mathcal{R}(\mathbf{x})_{\alpha+\ell}, \dots, \mathcal{R}(\mathbf{x})_{\alpha+k\ell+1} - \mathcal{R}(\mathbf{x})_{\alpha+k\ell}) \\ = & (x_{\alpha+1}, x_{\alpha+\ell+1} - x_{\alpha+1}, \dots, x_{\alpha+(k-1)\ell+1} - x_{\alpha+(k-2)\ell+1}, -x_{\alpha+(k-1)\ell+1}), \end{split}$$

It holds that $\sum_{i} \Delta^{\alpha}(\mathbf{x})_{i} = 0$.

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It holds that $\sum_{i} \Delta^{\alpha}(\mathbf{x})_{i} = 0$.

• *Note:* If $\mathcal{R}(\mathbf{x})_i \xrightarrow{\text{substitute}} \mathcal{R}(\mathbf{x})'_i$, two read sub-derivatives are affected.

$$\mathcal{R}(\mathbf{x})_i' - \mathcal{R}(\mathbf{x})_i = \sum_k \Delta^{i-1 \mod \ell}(\mathbf{x})_k'$$

$$= -\sum_k \Delta^{i \mod \ell}(\mathbf{x})_k' \neq 0$$

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Takeaway

Given $\mathcal{R}(\mathbf{x})'$, can determine **error value** & **position upto** mod ℓ .



• Can an erroneous read sub-derivative reveal region of error?



• Can an erroneous read sub-derivative reveal region of error?

$$\mathcal{R}(\boldsymbol{x}) \xrightarrow{\text{error at } i_1} \mathcal{R}(\boldsymbol{x})' = (1, 1, 2, 3, 2, 1, 0, 0)$$



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•
$$\sum_k \Delta^0(\mathbf{x})_k' = -\sum_k \Delta^1(\mathbf{x})_k' = 1 \implies i_1 \mod \ell = 1 \implies i_1 \in \{1, 4, 7\}$$



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Example ($\ell = 3, \delta = 1$)

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$$\Delta^{0}(\mathbf{x})' = (\mathcal{R}(\mathbf{x})'_{1}, \mathcal{R}(\mathbf{x})'_{4} - \mathcal{R}(\mathbf{x})'_{1}, \mathcal{R}(\mathbf{x})'_{7} - \mathcal{R}(\mathbf{x})'_{6})$$

$$= (x'_{1}, x'_{4} - x'_{1}, -x'_{4})$$

$$= (1, 1, 1, -1)$$



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Left to right reconstruction:

►
$$x_1' = 1$$
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$$x'_4 = 1$$
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$$x_4' - x_1' = 1 \implies x_1' = 0$$



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$$x_4' - x_1' = 1 \implies x_1' = 0$$

$$> x_1' = 1X$$



• Can an erroneous read sub-derivative reveal region of error?

Example ($\ell = 3, \delta = 1$)

$$\mathcal{R}(\textbf{\textit{x}}) \xrightarrow{\text{error at } \dot{h}} \mathcal{R}(\textbf{\textit{x}})' = (1,1,2,3,2,1,0,0)$$

•
$$\sum_k \Delta^0(\mathbf{x})'_k = -\sum_k \Delta^1(\mathbf{x})'_k = 1 \implies i_1 \mod \ell = 1 \implies i_1 \in \{1, 4, 7\} \implies i_1 \in \{1, 4\}$$

$$\begin{split} \Delta^0(\boldsymbol{x})' &= (\mathcal{R}(\boldsymbol{x})_1', \mathcal{R}(\boldsymbol{x})_4' - \mathcal{R}(\boldsymbol{x})_1', \mathcal{R}(\boldsymbol{x})_7' - \mathcal{R}(\boldsymbol{x})_6') \\ &= (\quad x_1' \quad , \quad x_4' - x_1' \quad , \quad -x_4' \quad) \\ &= (\quad 1 \quad , \quad 1 \quad , \quad -1 \quad) \end{split}$$

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Right to left reconstruction:

►
$$x_4' = 1$$
.

$$x_4' - x_1' = 1 \implies x_1' = 0$$

$$> x_1' = 1X$$



$$\mathcal{R}(\boldsymbol{x}) \xrightarrow{\text{error at } i_2} \mathcal{R}(\boldsymbol{x})' = (1, 1, 2, 2, 2, 1, 1, 0)$$

$$\bullet \ \textstyle \sum_k \Delta^0(\textbf{\textit{x}})_k' = -\sum_k \Delta^1(\textbf{\textit{x}})_k' = 1 \implies \textit{i}_2 \bmod \ell = 1 \implies \textit{i}_2 \in \{1,4,7\}.$$



Example ($\ell = 3, \delta = 1$)

$$\mathcal{R}(\boldsymbol{x}) \xrightarrow{\text{error at } i_2} \mathcal{R}(\boldsymbol{x})' = (1, 1, 2, 2, 2, 1, 1, 0)$$

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$$\begin{split} \Delta^0(\boldsymbol{x})' &= (\mathcal{R}(\boldsymbol{x})_1', \mathcal{R}(\boldsymbol{x})_4' - \mathcal{R}(\boldsymbol{x})_1', \mathcal{R}(\boldsymbol{x})_7' - \mathcal{R}(\boldsymbol{x})_6') \\ &= (\quad x_1' \quad , \quad x_4' - x_1' \quad , \quad -x_4' \quad) \\ &= (\quad 1 \quad , \quad 0 \quad , \quad 0 \quad) \end{split}$$



Example ($\ell = 3, \delta = 1$)

$$\mathcal{R}(\boldsymbol{x}) \xrightarrow{\text{error at } i_2} \mathcal{R}(\boldsymbol{x})' = (1, 1, 2, 2, 2, 1, 1, 0)$$

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- Left to right reconstruction:
 - ► $x_1' = 1$.



Example ($\ell = 3, \delta = 1$)

$$\mathcal{R}(\mathbf{x}) \xrightarrow{\text{error at } i_2} \mathcal{R}(\mathbf{x})' = (1, 1, 2, 2, 2, 1, 1, 0)$$

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• Left to right reconstruction:

►
$$x_1' = 1$$
.

$$x_4' - x_1' = 0 \implies x_4' = 1$$



Example ($\ell = 3, \delta = 1$)

$$\mathcal{R}(\mathbf{x}) \xrightarrow{\text{error at } i_2} \mathcal{R}(\mathbf{x})' = (1, 1, 2, 2, 2, 1, 1, 0)$$

 $\bullet \ \textstyle \sum_k \Delta^0(\textbf{\textit{x}})_k' = -\sum_k \Delta^1(\textbf{\textit{x}})_k' = 1 \implies \textit{i}_2 \bmod \ell = 1 \implies \textit{i}_2 \in \{1,4,7\}.$

$$\Delta^{0}(\mathbf{x})' = (\mathcal{R}(\mathbf{x})'_{1}, \mathcal{R}(\mathbf{x})'_{4} - \mathcal{R}(\mathbf{x})'_{1}, \mathcal{R}(\mathbf{x})'_{7} - \mathcal{R}(\mathbf{x})'_{6})$$

$$= (x'_{1} , x'_{4} - x'_{1} , -x'_{4})$$

$$= (1 , 0 , 0)$$

• Left to right reconstruction:

►
$$x_1' = 1$$
.

$$x_4' - x_1' = 0 \implies x_4' = 1$$

$$-x_4' = 0 X$$



Example ($\ell = 3, \delta = 1$)

$$\mathcal{R}(\mathbf{x}) \xrightarrow{\text{error at } i_2} \mathcal{R}(\mathbf{x})' = (1, 1, 2, 2, 2, 1, 1, 0)$$

•
$$\sum_k \Delta^0(\mathbf{x})_k' = -\sum_k \Delta^1(\mathbf{x})_k' = 1 \implies i_2 \mod \ell = 1 \implies i_2 \in \{1, 4, 7\}.$$

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$$= (x'_{1} , x'_{4} - x'_{1} , -x'_{4})$$

$$= (1 , 0 , 0)$$

• Left to right reconstruction:

►
$$x_1' = 1$$
.

$$x_4' - x_1' = 0 \implies x_4' = 1$$

$$-x_4'=0$$
 X

• Right to left reconstruction:

►
$$x_4' = 0$$
.



Example ($\ell = 3, \delta = 1$)

$$\mathcal{R}(\mathbf{x}) \xrightarrow{\text{error at } i_2} \mathcal{R}(\mathbf{x})' = (1, 1, 2, 2, 2, 1, 1, 0)$$

•
$$\sum_k \Delta^0(\mathbf{x})_k' = -\sum_k \Delta^1(\mathbf{x})_k' = 1 \implies i_2 \mod \ell = 1 \implies i_2 \in \{1, 4, 7\}.$$

• Left to right reconstruction:

►
$$x_1' = 1$$
.

$$x_4' - x_1' = 0 \implies x_4' = 1$$

$$-x_{A}'=0$$
 X

• Right to left reconstruction:

$$x_4' = 0.$$

$$> x_4' - x_1' = 0 \implies x_1' = 0$$



Example ($\ell = 3, \delta = 1$)

$$\mathcal{R}(\mathbf{x}) \xrightarrow{\text{error at } i_2} \mathcal{R}(\mathbf{x})' = (1, 1, 2, 2, 2, 1, 1, 0)$$

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$$= (x'_{1} , x'_{4} - x'_{1} , -x'_{4})$$

$$= (1 , 0 , 0)$$

• Left to right reconstruction:

►
$$x_1' = 1$$
.

$$x_4' - x_1' = 0 \implies x_4' = 1$$

$$-x_4' = 0 X$$

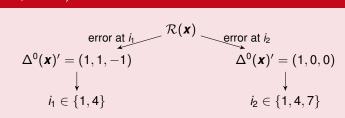
• Right to left reconstruction:

$$x_4' = 0.$$

$$x_4' - x_1' = 0 \implies x_1' = 0$$

►
$$x_1' = 1X$$







Example ($\ell = 3, \delta = 1$)

error at
$$i_1$$
 $\mathcal{R}(\boldsymbol{x})$ error at i_2 $\Delta^0(\boldsymbol{x})' = (1,1,-1)$ $\Delta^0(\boldsymbol{x})' = (1,0,0)$ \vdots $i_2 \in \{1,4,7\}$

$$\Delta^{0}(\mathbf{x}) = (1 \quad 0 \quad 0 \quad 0 \quad \cdots \quad 0 \quad -1)$$

$$x_{1} = 1 \quad x_{4} = 1 \quad x_{7} = 1 \quad x_{11} = 1 \quad \cdots \quad x_{\lfloor \frac{n-1}{3} \rfloor 3+1} = 1$$



Example ($\ell = 3, \delta = 1$)

$$\Delta^{0}(\mathbf{x})' = (1 \quad 0 \quad -1 \quad 0 \quad \cdots \quad 0 \quad -1)$$

$$x_{1} = 1 \quad x_{4} = 1 \quad x_{7} = 1 \quad x_{11} = 1 \quad \cdots \quad x_{\lfloor \frac{n-1}{3} \rfloor 3+1} = 1$$

$$x'_{1} = 1 \quad x'_{4} = 1 \quad x'_{7} = 0 \quad x'_{11} = 0 \quad \cdots \quad x'_{\lfloor \frac{n-1}{3} \rfloor 3+1} = 0$$



Example ($\ell = 3, \delta = 1$)

$$\Delta^{0}(\mathbf{x})' = (1 \quad 0 \quad -1 \quad 0 \quad \cdots \quad 0 \quad -1)$$

$$x_{1} = 1 \quad x_{4} = 1 \quad x_{7} = 1 \quad x_{11} = 1 \quad \cdots \quad x_{\lfloor \frac{n-1}{3} \rfloor 3+1} = 1$$

$$x'_{1} = 1 \quad x'_{4} = 1 \quad x'_{7} = 0 \quad x'_{11} = 0 \quad \cdots \quad x'_{\lfloor \frac{n-1}{3} \rfloor 3+1} = 0$$

• Run of 0s delays error detection \rightarrow restrict run-length of 0s in all $\Delta^{\alpha}(\mathbf{x})!$

Error-correcting Code



• restrict run-length of 0s in all read sub-derivatives,

Construction

$$\mathcal{C}(n,\ell) = \{ \boldsymbol{x} \in \Sigma_2^n : \Delta(\boldsymbol{x}) \bmod 2 \in RLL(\log 2(n+\ell)),$$

where
$$\Delta(\mathbf{x}) = \Delta^{0}(\mathbf{x}) \circ \Delta^{1}(\mathbf{x}) \circ \cdots \circ \Delta^{\ell-1}(\mathbf{x})$$

C. Schoeny *et al.*, "Codes correcting a burst of deletions or insertions," *IEEE Trans. Inf. Theory*, vol. 63, no. 4, pp. 1971–1985, Apr. 2017

Error-correcting Code



- restrict run-length of 0s in all read sub-derivatives,
- Correct 1 substitution in length-a window with folded Hamming code $\mathcal{H}(n, a)$:

$$\begin{bmatrix}
\mathbf{H}_{a} & \mathbf{H}_{a} & \cdots & \mathbf{H}_{a} \\
\frac{n}{2^{a}-1} & \text{times}
\end{bmatrix}$$

where \mathbf{H}_a corresponds to Hamming code of order a.

Construction

$$\mathcal{C}(n,\ell) = \{ \boldsymbol{x} \in \Sigma_2^n : \Delta(\boldsymbol{x}) \bmod 2 \in RLL(\log 2(n+\ell)), \\ \mathcal{R}^{\pi}(\boldsymbol{x}) \bmod 2 \in \mathcal{H}(n+\ell-1,\log\log 8(n+\ell)+1) \},$$

where $\Delta(\mathbf{x}) = \Delta^0(\mathbf{x}) \circ \Delta^1(\mathbf{x}) \circ \cdots \circ \Delta^{\ell-1}(\mathbf{x})$ and $\mathcal{R}^{\pi}(\mathbf{x})$ is a permutation of $\mathcal{R}(\mathbf{x})$.

C. Schoeny et al., "Codes correcting a burst of deletions or insertions," IEEE Trans. Inf. Theory, vol. 63, no. 4, pp. 1971–1985, Apr. 2017

Error-correcting Code



- restrict run-length of 0s in all read sub-derivatives,
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$$\underbrace{\begin{bmatrix} \mathbf{H}_a & \mathbf{H}_a & \cdots & \mathbf{H}_a \end{bmatrix}}_{\frac{n}{2^a-1} \text{ times}}$$

where \mathbf{H}_a corresponds to Hamming code of order a.

Construction

$$\mathcal{C}(n,\ell) = \{ \boldsymbol{x} \in \Sigma_2^n : \Delta(\boldsymbol{x}) \bmod 2 \in RLL(\log 2(n+\ell)), \\ \mathcal{R}^{\pi}(\boldsymbol{x}) \bmod 2 \in \mathcal{H}(n+\ell-1,\log\log 8(n+\ell)+1) \},$$

where
$$\Delta(\mathbf{x}) = \Delta^0(\mathbf{x}) \circ \Delta^1(\mathbf{x}) \circ \cdots \circ \Delta^{\ell-1}(\mathbf{x})$$
 and $\mathcal{R}^{\pi}(\mathbf{x})$ is a permutation of $\mathcal{R}(\mathbf{x})$.

 \rightarrow Requires $\log \log n + o(1)$ redundant bits (optimal up to a constant).

C. Schoeny et al., "Codes correcting a burst of deletions or insertions," *IEEE Trans. Inf. Theory*, vol. 63, no. 4, pp. 1971–1985, Apr. 2017

Introduction

Channel Mode

Minimum Redundancy

Error-correcting Code

Conclusion

Summary



Results

For a simplified model of nanopore sequencing,

- Established that $\log \log n$ redundancy needed to correct 1 substitution
- Proposed an error-correcting construction that is optimal up to a constant.

Future work

- Multiple substitutions
- Deletions
- Extension to non-binary, $\delta > 1$.

Thank you!

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Example ($\ell = 3, \delta = 1$)

We receive $\mathcal{R}(\mathbf{x})' = (0, 1, 3, 2, 2, 2, 1, 0, 0)$.



Example $(\ell = 3, \delta = 1)$

We receive
$$\mathcal{R}(\mathbf{x})' = (0, 1, 3, 2, 2, 2, 1, 0, 0)$$
.

• $|\mathcal{R}(\mathbf{x})_3' - \mathcal{R}(\mathbf{x})_2'| \leq 1 \rightarrow \text{Error pos. 2 or 3.}$



We receive
$$\mathcal{R}(\mathbf{x})' = (\mathbf{0}, 1, 3, 2, 2, 2, 1, 0, 0)$$
.

- $|\mathcal{R}(\mathbf{x})_3' \mathcal{R}(\mathbf{x})_2'| \leq 1 \rightarrow \text{Error pos. 2 or 3.}$
- Left-to-right reconstruction:

►
$$\mathcal{R}(x)_1 = \text{wt}(x_1) = 0 \to x_1 = 0$$



We receive
$$\mathcal{R}(\mathbf{x})' = (0, 1, 3, 2, 2, 2, 1, 0, 0)$$
.

- $|\mathcal{R}(\mathbf{x})_3' \mathcal{R}(\mathbf{x})_2'| \leq 1 \rightarrow \text{Error pos. 2 or 3.}$
- Left-to-right reconstruction:
 - ▶ $\mathcal{R}(x)_1 = \text{wt}(x_1) = 0 \rightarrow x_1 = 0$
 - $ightharpoonup \mathcal{R}(x)_2 = \operatorname{wt}(x_1^2) = 1 \to x_2 = 1$



We receive
$$\mathcal{R}(\mathbf{x})' = (0, 1, 3, 2, 2, 2, 1, 0, 0)$$
.

- $|\mathcal{R}(\mathbf{x})_3' \mathcal{R}(\mathbf{x})_2'| \leq 1 \rightarrow \text{Error pos. 2 or 3.}$
- Left-to-right reconstruction:

▶
$$\mathcal{R}(x)_1 = \text{wt}(x_1) = 0 \rightarrow x_1 = 0$$

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▶
$$\mathcal{R}(\mathbf{x})_3 = \text{wt}(\mathbf{x}_1^3) = 3 \to x_3 = 2 \notin \{0, 1\} \to \text{Error pos. 3.}$$



Example $(\ell = 3, \delta = 1)$

We receive
$$\mathcal{R}(\mathbf{x})' = (0, 1, \circledast, 2, 2, 2, 1, 0, 0)$$
.

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- Left-to-right reconstruction:

▶
$$\mathcal{R}(x)_1 = \text{wt}(x_1) = 0 \rightarrow x_1 = 0$$

$$ightharpoonup \mathcal{R}(x)_2 = \text{wt}(x_1^2) = 1 \to x_2 = 1$$

▶
$$\mathcal{R}(\mathbf{x})_3 = \text{wt}(\mathbf{x}_1^3) = 3 \to x_3 = 2 \notin \{0, 1\} \to \text{Error pos. 3.}$$

Consider erasure.



We receive
$$\mathcal{R}(\mathbf{x})' = (0, 1, \circledast, 2, 2, 2, 1, 0, 0)$$
.

- $|\mathcal{R}(\mathbf{x})_3' \mathcal{R}(\mathbf{x})_2'| \leq 1 \rightarrow \text{Error pos. 2 or 3.}$
- Left-to-right reconstruction:

▶
$$\mathcal{R}(x)_1 = \text{wt}(x_1) = 0 \to x_1 = 0$$

$$ightharpoonup \mathcal{R}(x)_2 = \text{wt}(x_1^2) = 1 \to x_2 = 1$$

▶
$$\mathcal{R}(\mathbf{x})_3 = \text{wt}(\mathbf{x}_1^3) = 3 \to x_3 = 2 \notin \{0, 1\} \to \text{Error pos. 3.}$$

- · Consider erasure.
- $\sum_{i} \mathcal{R}(\mathbf{x})_{i} \mod \ell = 0$



We receive
$$\mathcal{R}(\mathbf{x})' = (0, 1, 1, 2, 2, 2, 1, 0, 0)$$
.

- $|\mathcal{R}(\mathbf{x})_3' \mathcal{R}(\mathbf{x})_2'| \leq 1 \rightarrow \text{Error pos. 2 or 3.}$
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- $\sum_{i} \mathcal{R}(\mathbf{x})_{i} \mod \ell = 0 \rightarrow \mathcal{R}(\mathbf{x})_{3} = 1.$



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We receive
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.

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- Left-to-right reconstruction:

▶
$$\mathcal{R}(x)_1 = \text{wt}(x_1) = 0 \rightarrow x_1 = 0$$

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$$ightharpoonup \mathcal{R}(x)_3 = \text{wt}(x_1^3) = 3 \to x_3 = 2 \notin \{0,1\} \to \text{Error pos. 3.}$$

- · Consider erasure.
- $\sum_{i} \mathcal{R}(\mathbf{x})_{i} \mod \ell = 0 \rightarrow \mathcal{R}(\mathbf{x})_{3} = 1.$

Takeaway

If error magnitude> 1, can correct immediately.

→ Sufficient to consider ±1 errors!