Stanford

Improved read/write cost tradeoff in DNA-based data storage using LDPC codes

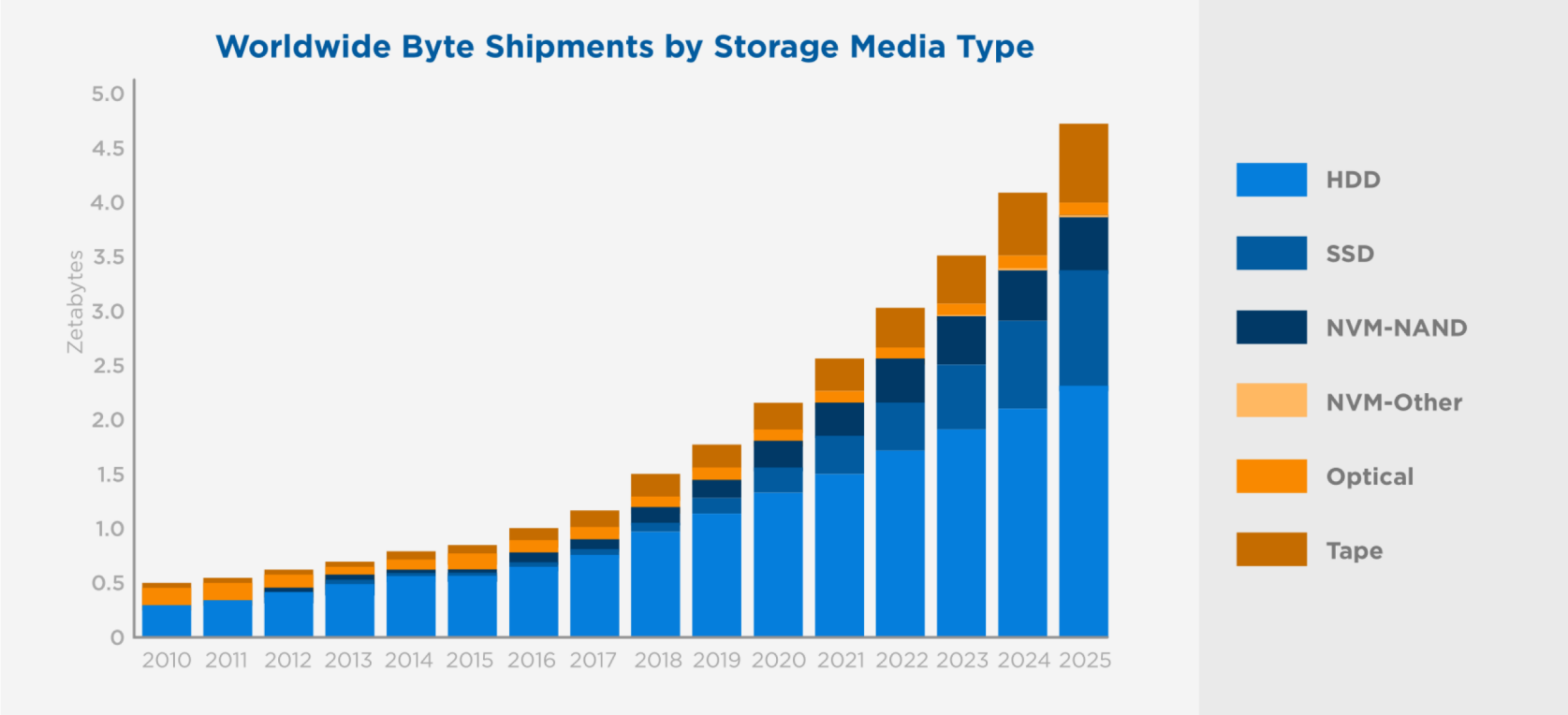
Shubham Chandak
Stanford University
Allerton 2019

Outline

- Motivation
- DNA storage setup
- Theoretical analysis
- Proposed framework
- Results
- Conclusions

Motivation

The amount of stored data is growing exponentially:



Source: Data Age 2025, sponsored by Seagate with data from IDC Global DataSphere, Nov 2018

Source: https://www.seagate.com/our-story/data-age-2025/

200 Petabyte

200 Petabyte

40,000 x 5 TByte HDDs
40 tons

10s of years

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DNA
1 gram

1,000s of years

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40,000 x 5 TByte HDDs
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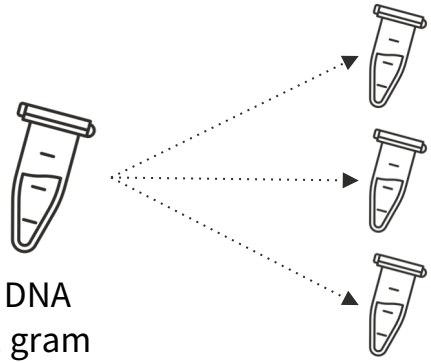
10s of years



DNA
1 gram

1,000s of years

Easy duplication

July 2, 2019

Hot News for the Summer from CATALOG

POSTED BY : SEAN MIHM / 0 COMMENTS / UNDER : UNCATEGORIZED

CATALOG Encodes Wikipedia Into DNA!

https://catalogdna.com/uncategorized/hot-news-for-the-summer-from-catalog/

DNA storage setup

How to store data in DNA sequences?

File

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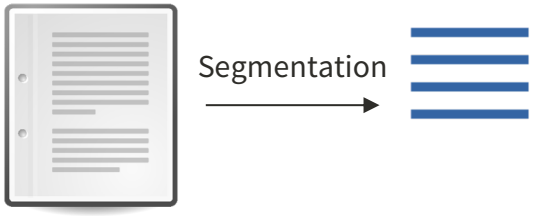
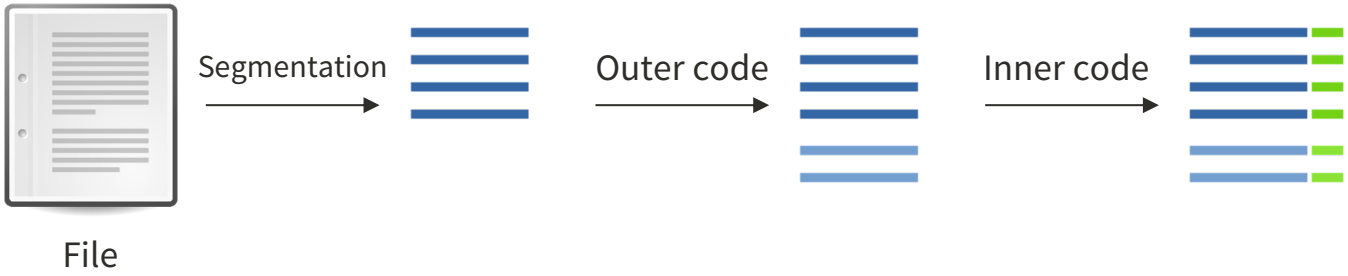


How to store data in DNA sequences?



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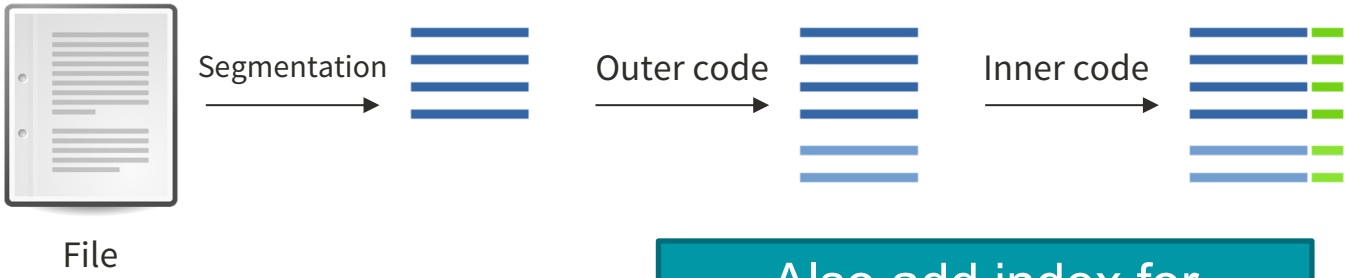
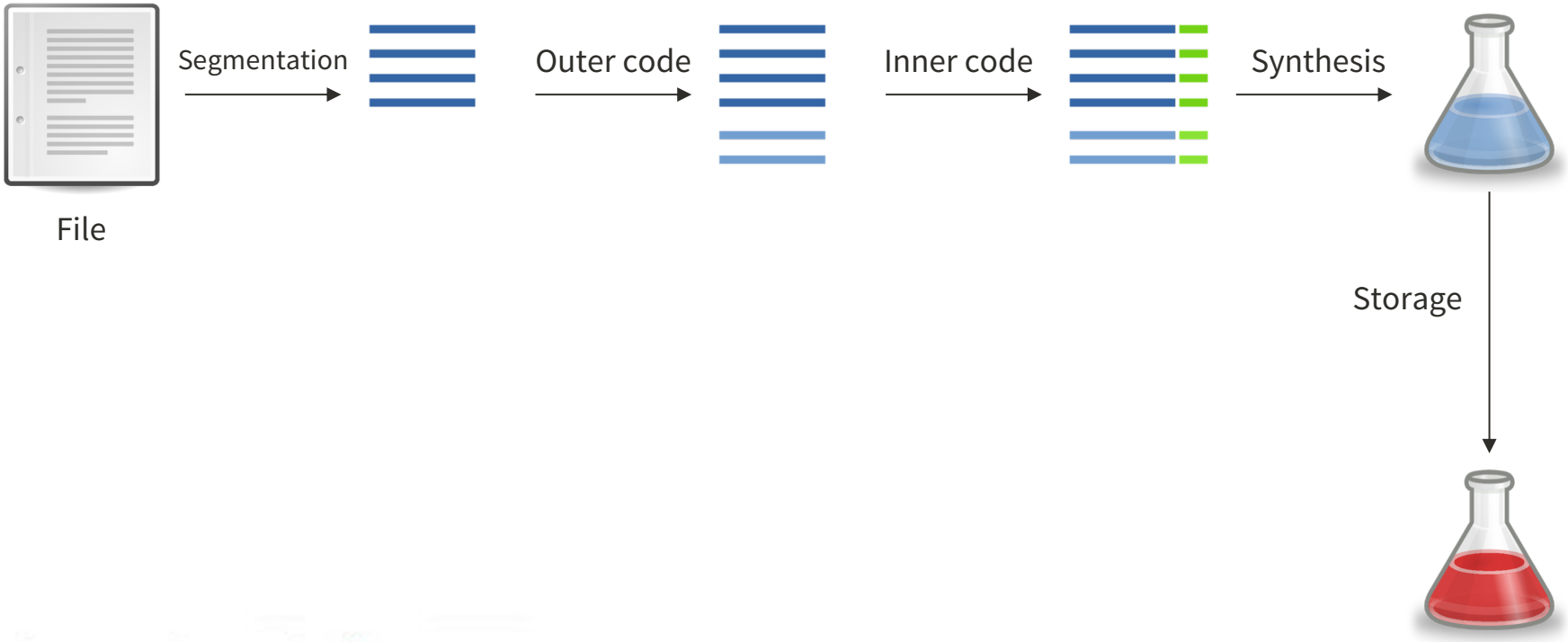


Also add index for recovering order of segments

How to store data in DNA sequences?



CustomArray | GenScript Make Research Easy

http://www.customarrayinc.com/

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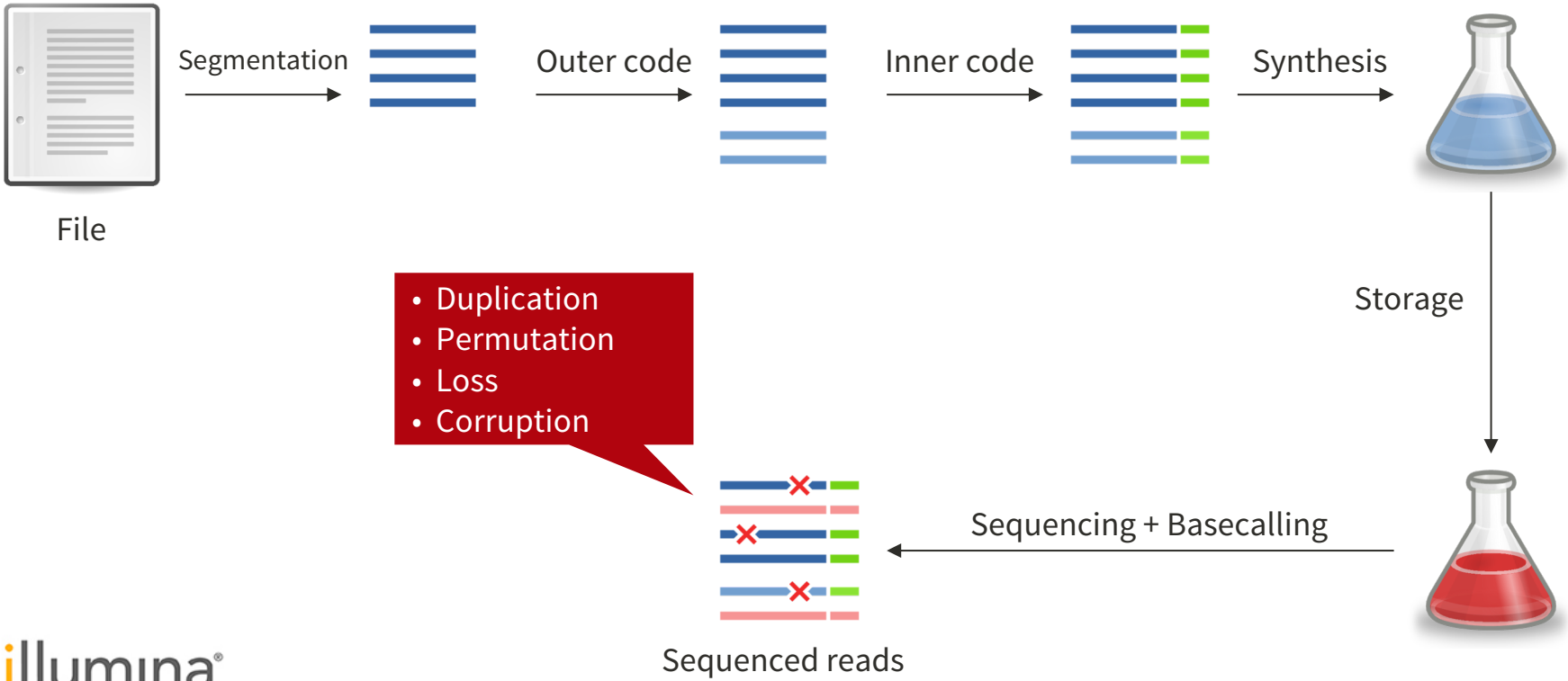
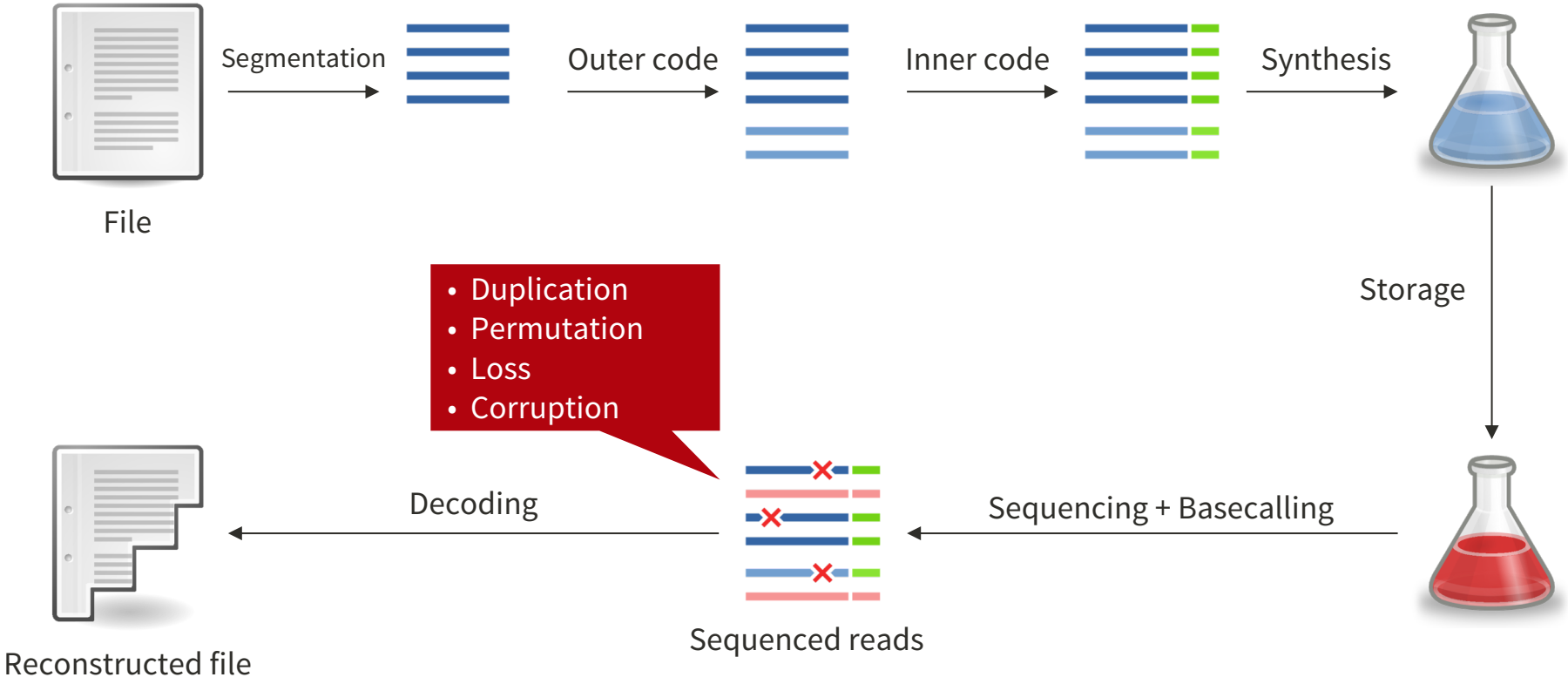
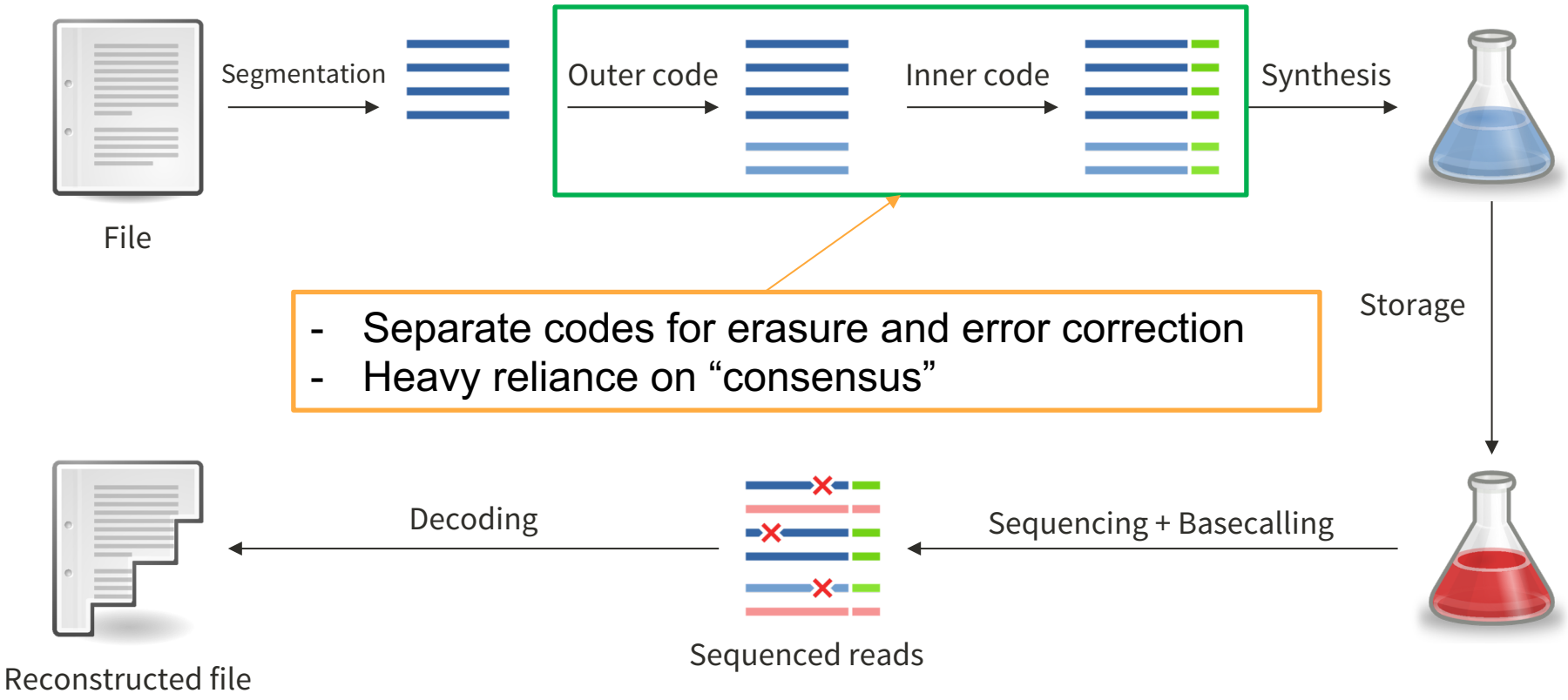


illumina®

How to store data in DNA sequences?



How to store data in DNA sequences?



Previous works

- Multiple previous works focusing on:
  - Error correction coding
  - Random access to subsets of synthesized sequences using PCR primers
  - Scalable and cost effective synthesis techniques
  - Different sequencing platforms
  - Theoretical analysis

1. Yazdi, SM Hossein Tabatabaei, et al. "A rewritable, random-access DNA-based storage system." *Scientific reports* 5 (2015): 14138.
2. Erlich, Yaniv, and Dina Zielinski. "DNA Fountain enables a robust and efficient storage architecture." Science 355.6328 (2017): 950-954.
3. Organick, Lee, et al. "Random access in large-scale DNA data storage." Nature biotechnology 36.3 (2018): 242.
4. Blawat, Meinolf, et al. "Forward error correction for DNA data storage." Procedia Computer Science 80 (2016): 1011-1022.
5. Church, George M., Yuan Gao, and Sriram Kosuri. "Next-generation digital information storage in DNA." *Science* 337.6102 (2012): 1628-1628.
6. Heckel, Reinhard, et al. "Fundamental limits of DNA storage systems." *2017 IEEE International Symposium on Information Theory (ISIT)*. IEEE, 2017.
7. Tomek, Kyle J., et al. "Driving the scalability of DNA-based information storage systems." *ACS synthetic biology* (2019).
8. Lenz, Andreas, et al. "Coding over sets for DNA storage." *2018 IEEE International Symposium on Information Theory (ISIT)*. IEEE, 2018.
9. Lee, Henry H., et al. "Terminator-free template-independent enzymatic DNA synthesis for digital information storage." *Nature communications* 10.1 (2019): 2383.

Theoretical analysis

Read-write cost tradeoff

- Fundamental quantities from a coding theory perspective:
  - Writing cost (bases synthesized/message bit)
  - Reading cost (bases sequenced/message bit)
  - *Note*: “Coverage” (= bases sequenced/bases synthesized) doesn’t capture the actual reading cost.

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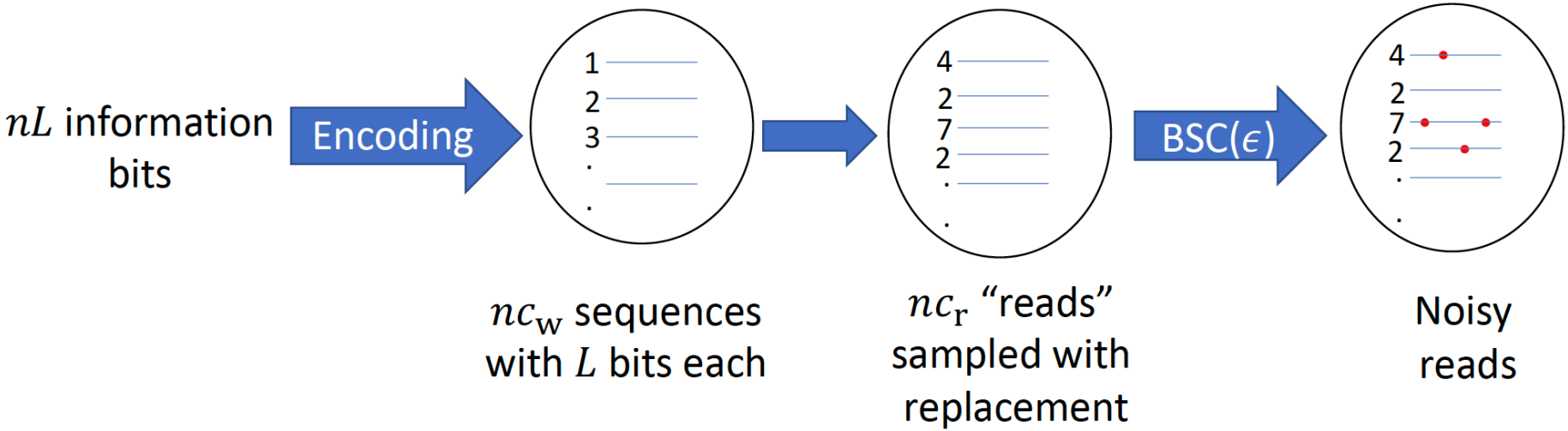
- Fixed sequence length means asymptotic information capacity = 0!
  - Previous works assumed sequence length growing logarithmically in number of sequences
  - Does not capture the limitations posed by short sequence length

Simplified model for analysis



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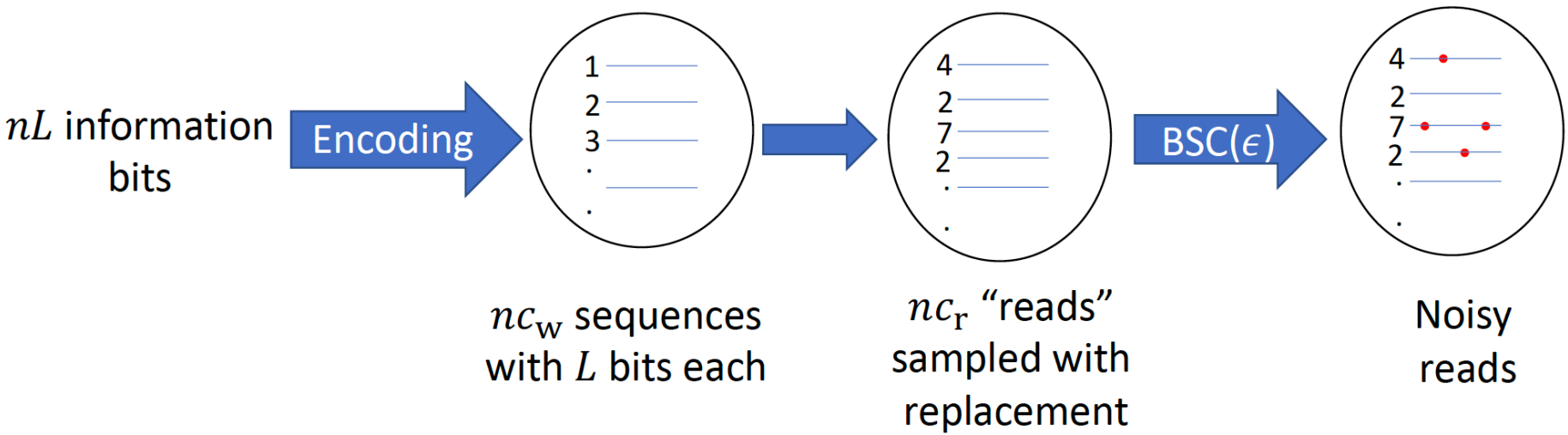


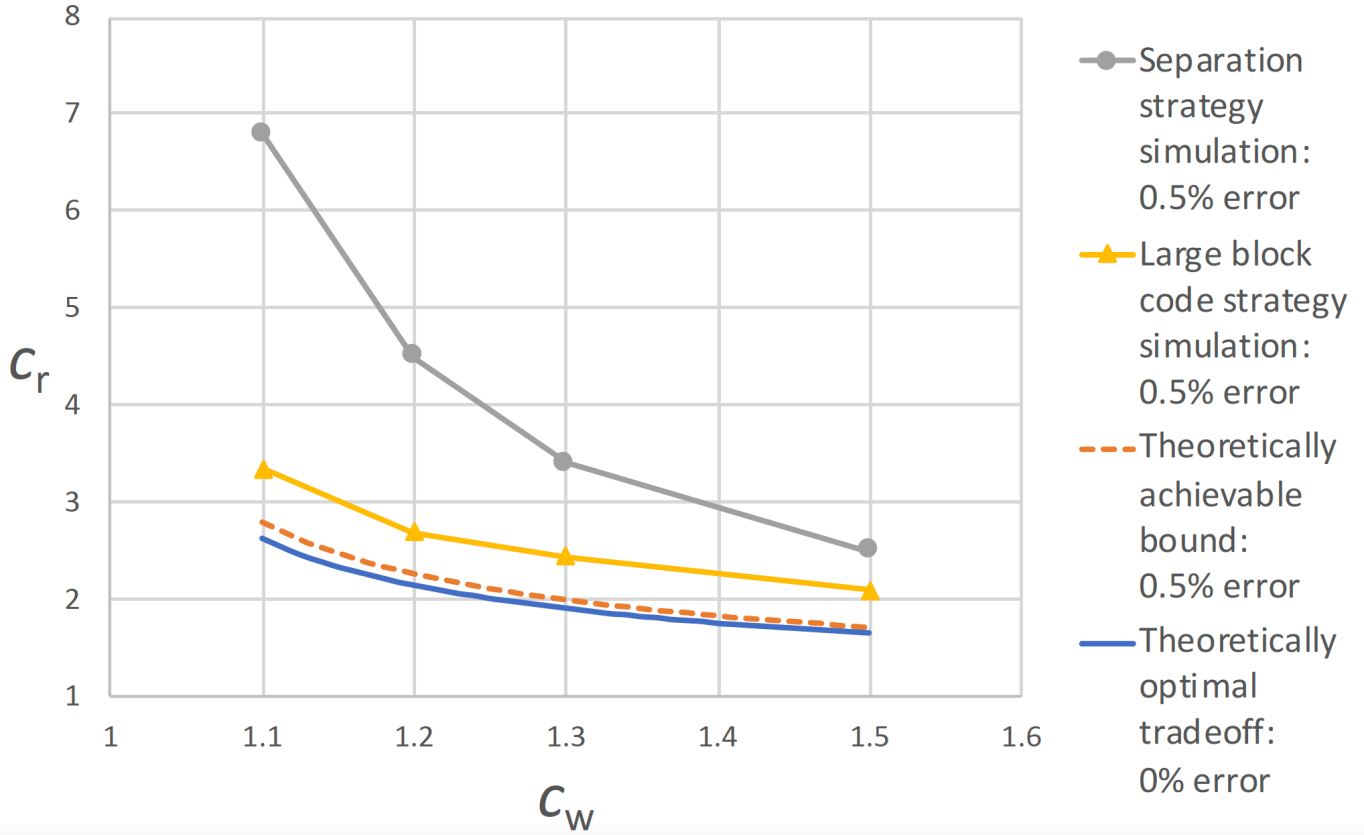
Use a memoryless approximation and obtain asymptotically achievable tradeoff between c_w and c_r

Two strategies

Strategy 1: Inner/outer code separation

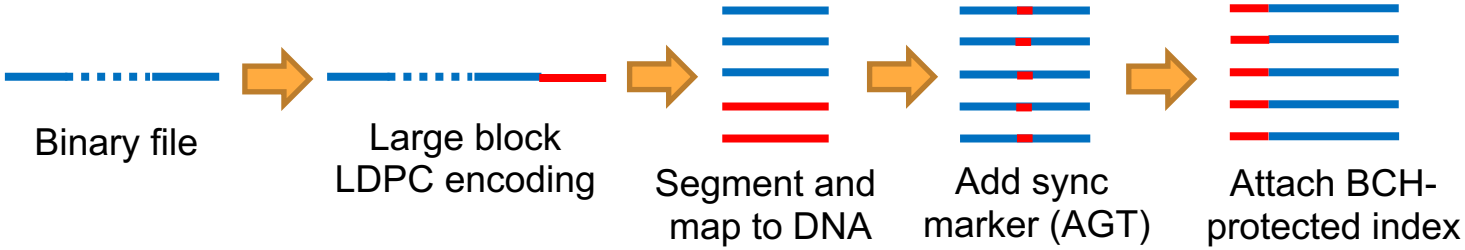
Strategy 2: Single large block code

Simulation results



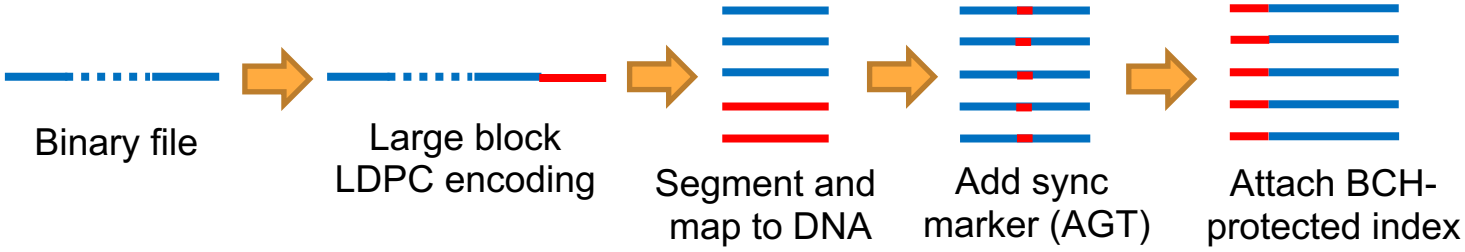
Proposed framework

Proposed approach



Encoding

Proposed approach



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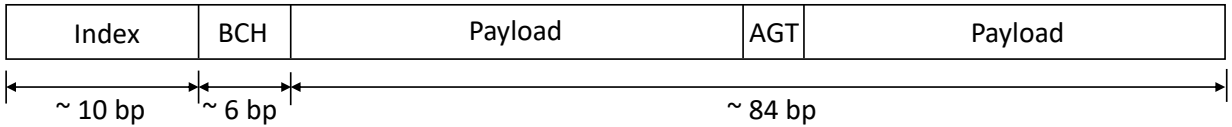

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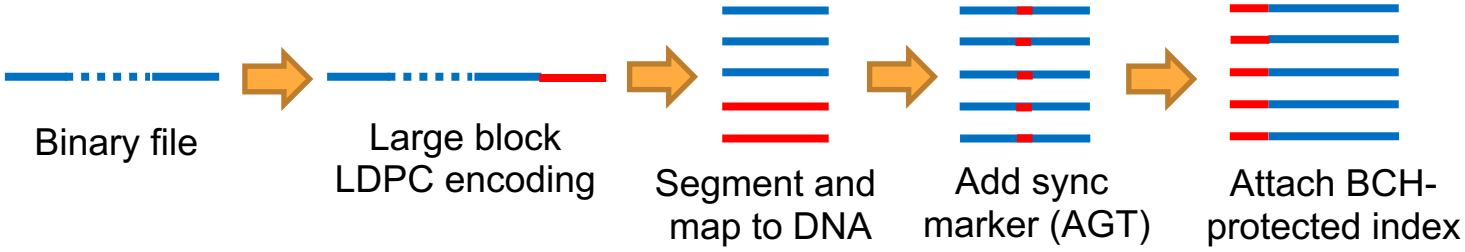

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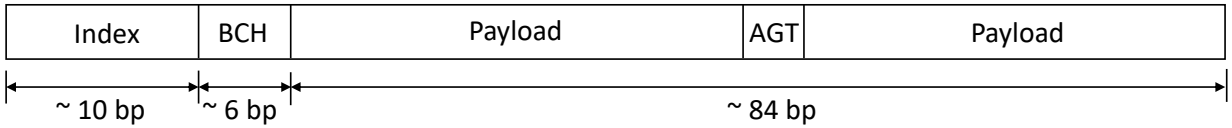
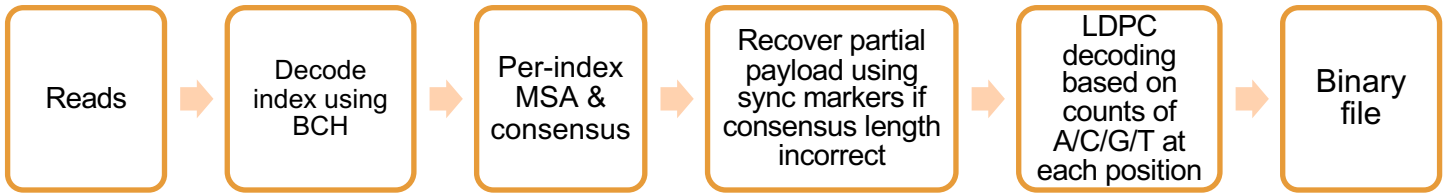




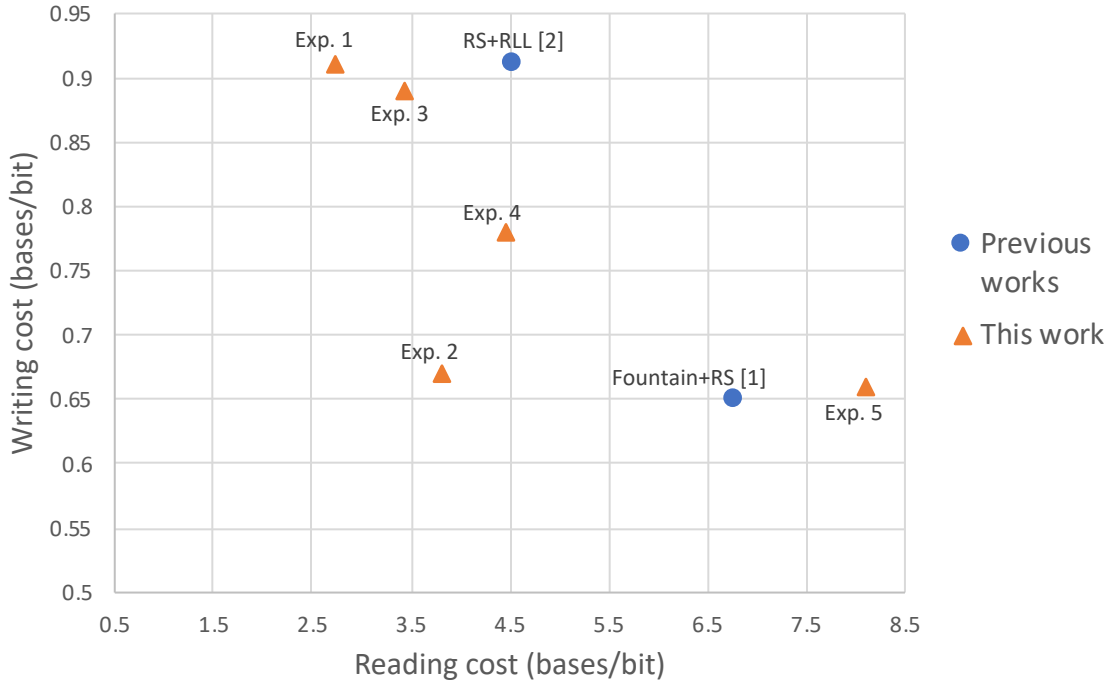
Decoding

Results

Experimental Parameters

- Multiple parameter experiments, storing around 200 KB data each.
- CustomArray synthesis, length 150 including primers.
- Sequenced with Illumina iSeq.
- Total error rate around 1.3% (substitution: 0.4%, deletion: 0.85%, insertion: 0.05%) – *cheaper* and *noisier* synthesis as compared to previous works.

Experimental Results



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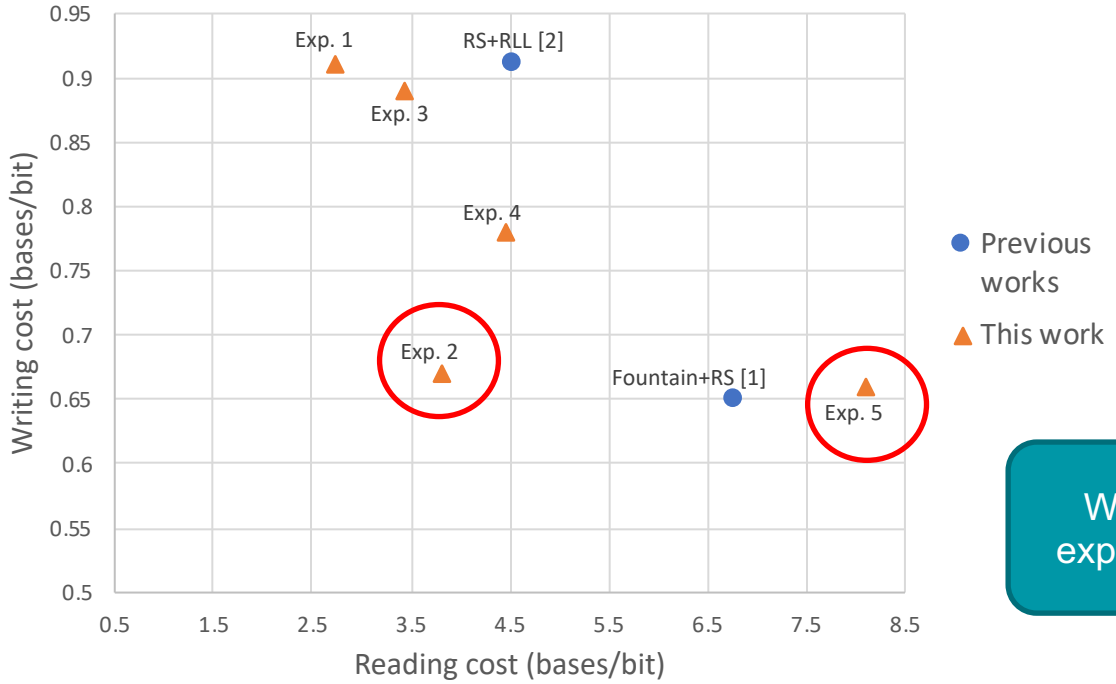

What happened in experiments 2 and 5?

1. Y. Erlich and D. Zielinski, “DNA Fountain enables a robust and efficient storage architecture," *Science*, vol. 355, no. 6328, pp. 950-954, 2017.
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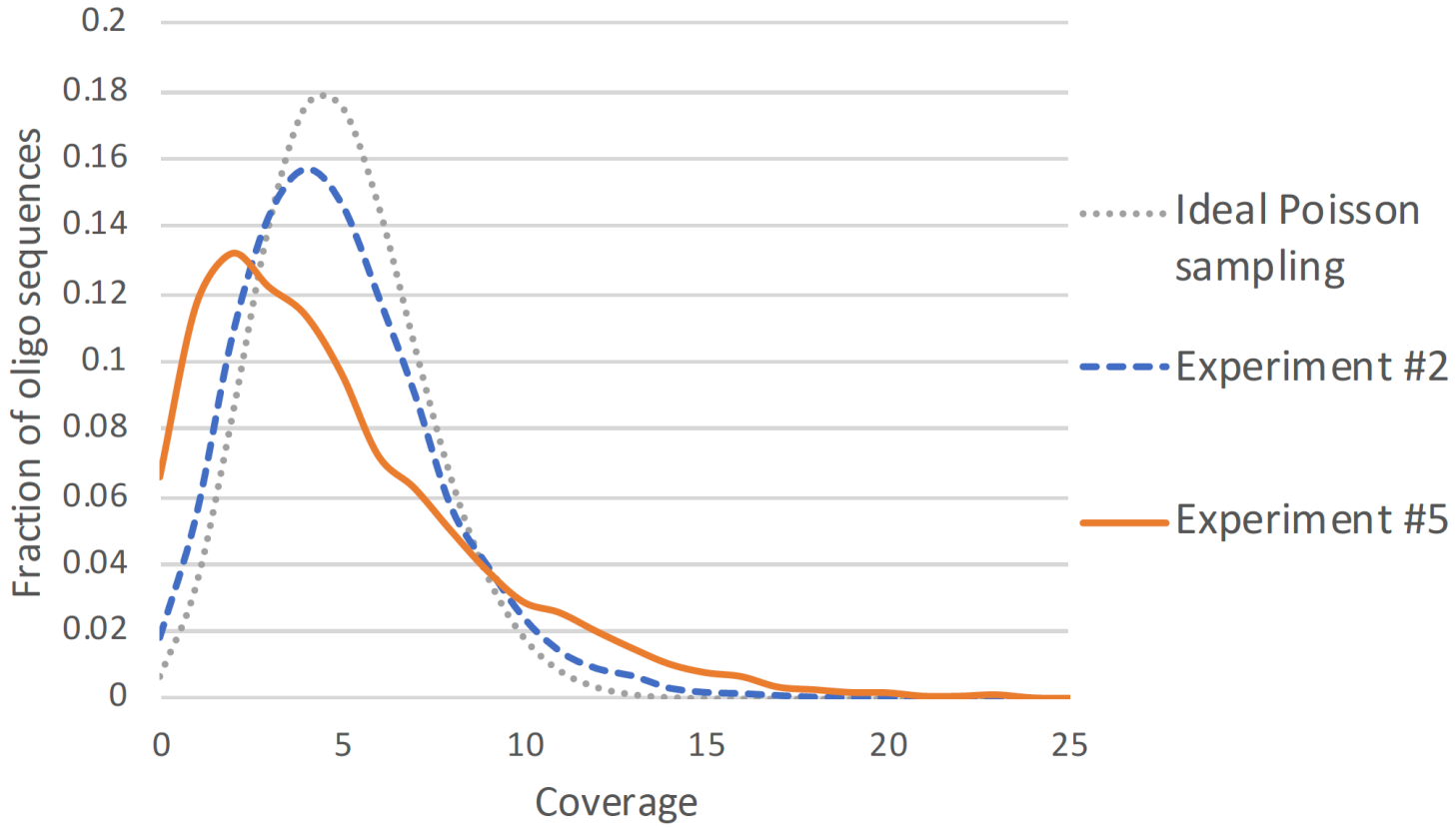
Coverage variation



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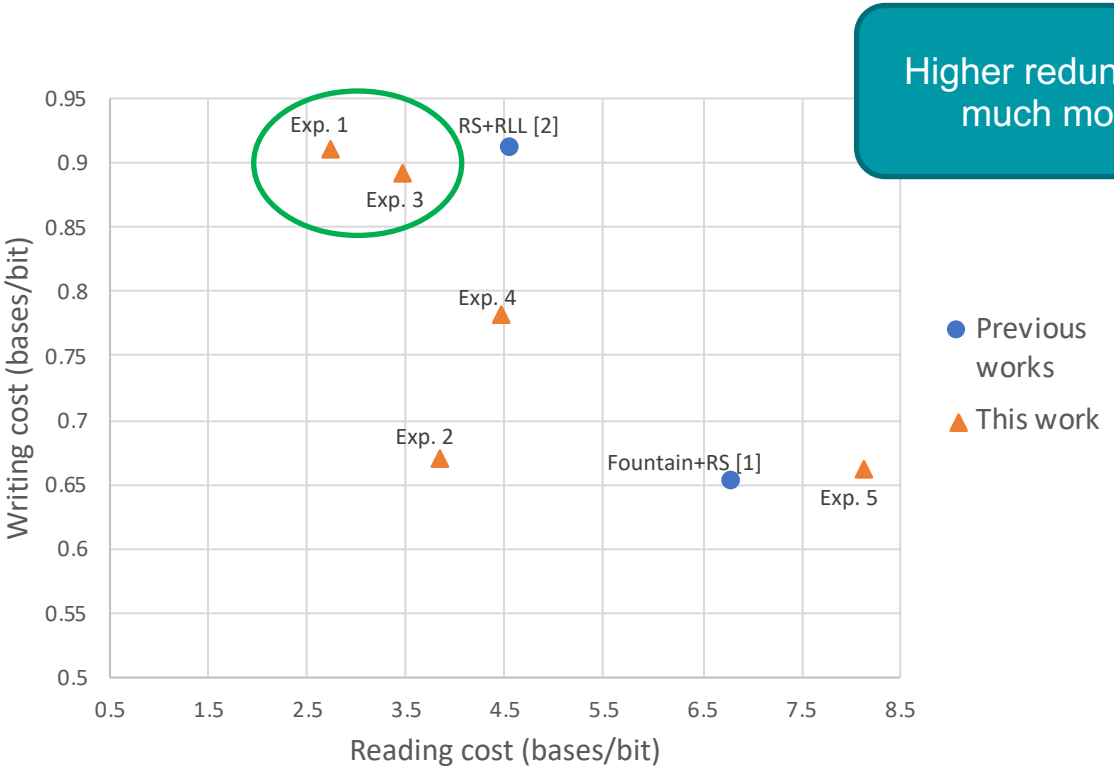

Experimental Results

Higher redundancy codes much more robust!

More analysis in paper

Conclusions

- Introduced novel coding schemes for Illumina sequencing based DNA storage
    - Improved read/write cost tradeoff despite noisier synthesis
- Code and data: https://github.com/shubhamchandak94/LDPC_DNA_storage
- Biorxiv: https://www.biorxiv.org/content/10.1101/770032v1

Future work

- Possibilities for improvement:
  - Optimized LDPC codes, e.g., using protographs
  - Better codes for insertion/deletion: LDPC with markers, VT codes
  - Check out q-ary VT codes implementation: https://github.com/shubhamchandak94/VT_codes/

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- Plan to integrate these with random access and repeated reading.
- Long term vision: Nanopore sequencing + cheaper and noisier synthesis techniques

Team and funding

Shubham Chandak

Kedar Tatwawadi

Joachim Neu

Jay Mardia

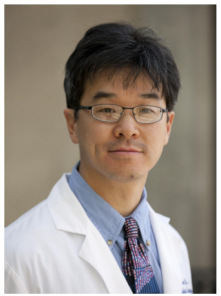
Billy Lau

Matt Kubit

Peter Griffin

Tsachy Weissman

Mary Wootters



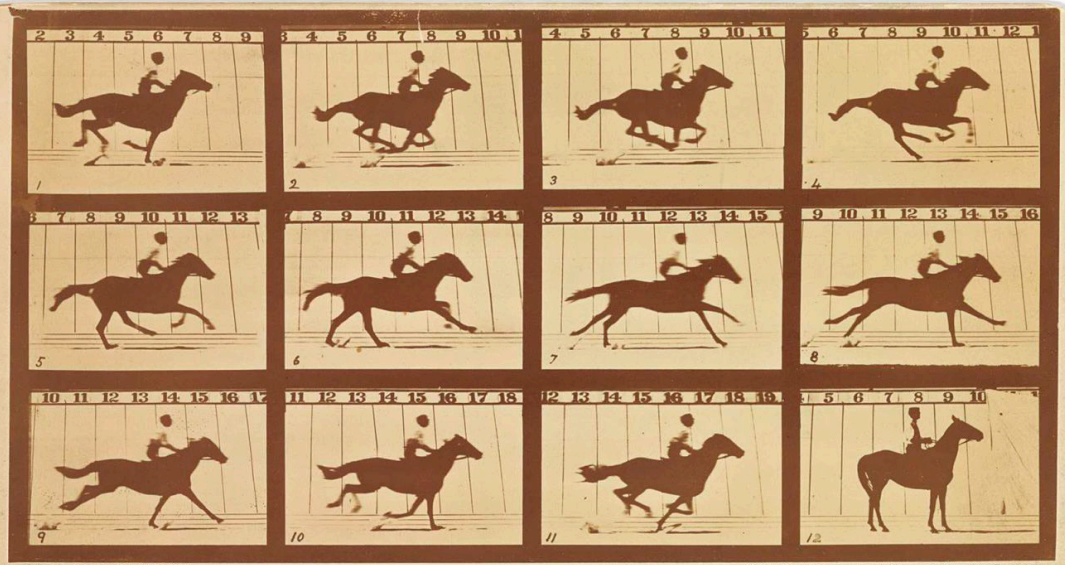
Hanlee Ji

SemiSynBio: Highly scalable random access DNA data storage with nanopore-based reading

Beckman Center Innovative Technology Seed Grant

Scalable Long-Term DNA Storage with Error Correction and Random-Access Retrieval

National Institutes of Health



MORSE'S Gallery, 417 Montgomery St., San Francisco

THE HORSE IN MOTION.

Illustrated by

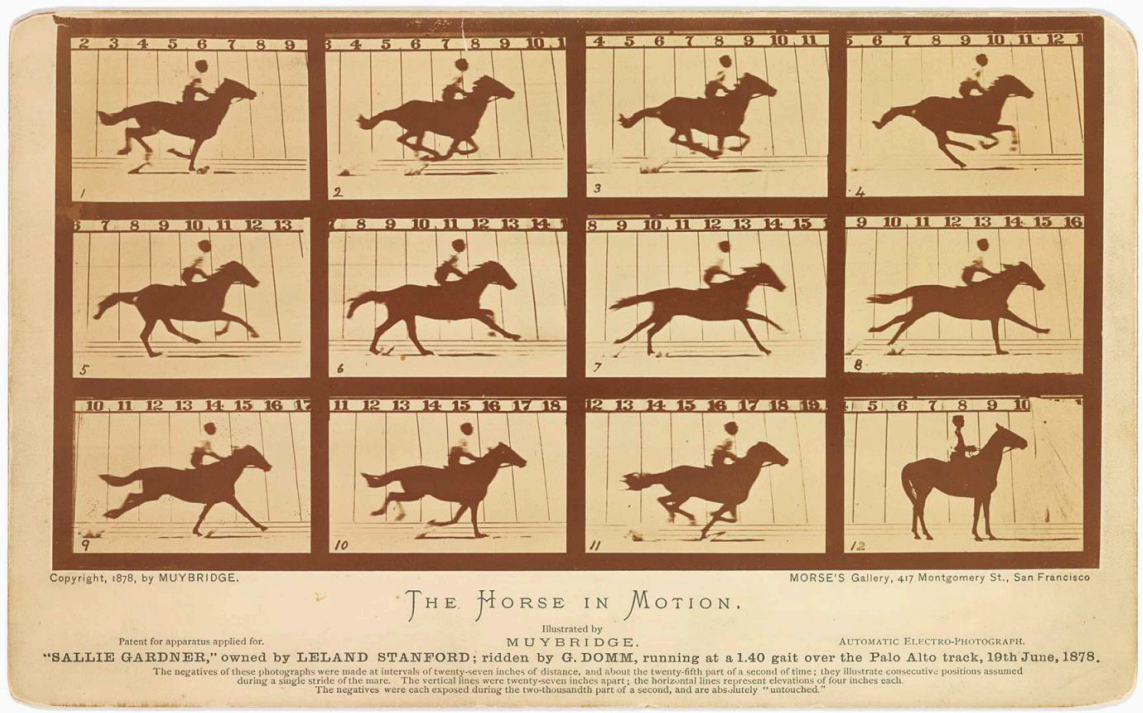
MUYBRIDGE.

Patent for apparatus applied for. AUTOMATIC ELECTRO-PHOTOGRAPH.

"SALLIE GARDNER," owned by LELAND STANFORD; ridden by G. DOMM, running at a 1.40 gait over the Palo Alto track, 19th June, 1878.

The negatives of these photographs were made at intervals of twenty-seven inches of distance, and about the twenty-fifth part of a second of time; they illustrate consecutive positions assumed during a single stride of the mare. The vertical lines were twenty-seven inches apart; the horizontal lines represent elevations of four inches each.
The negatives were each exposed during the two-thousandth part of a second, and are absolutely "untouched."

Thank You!



Biorxiv: https://www.biorxiv.org/content/10.1101/770032v1

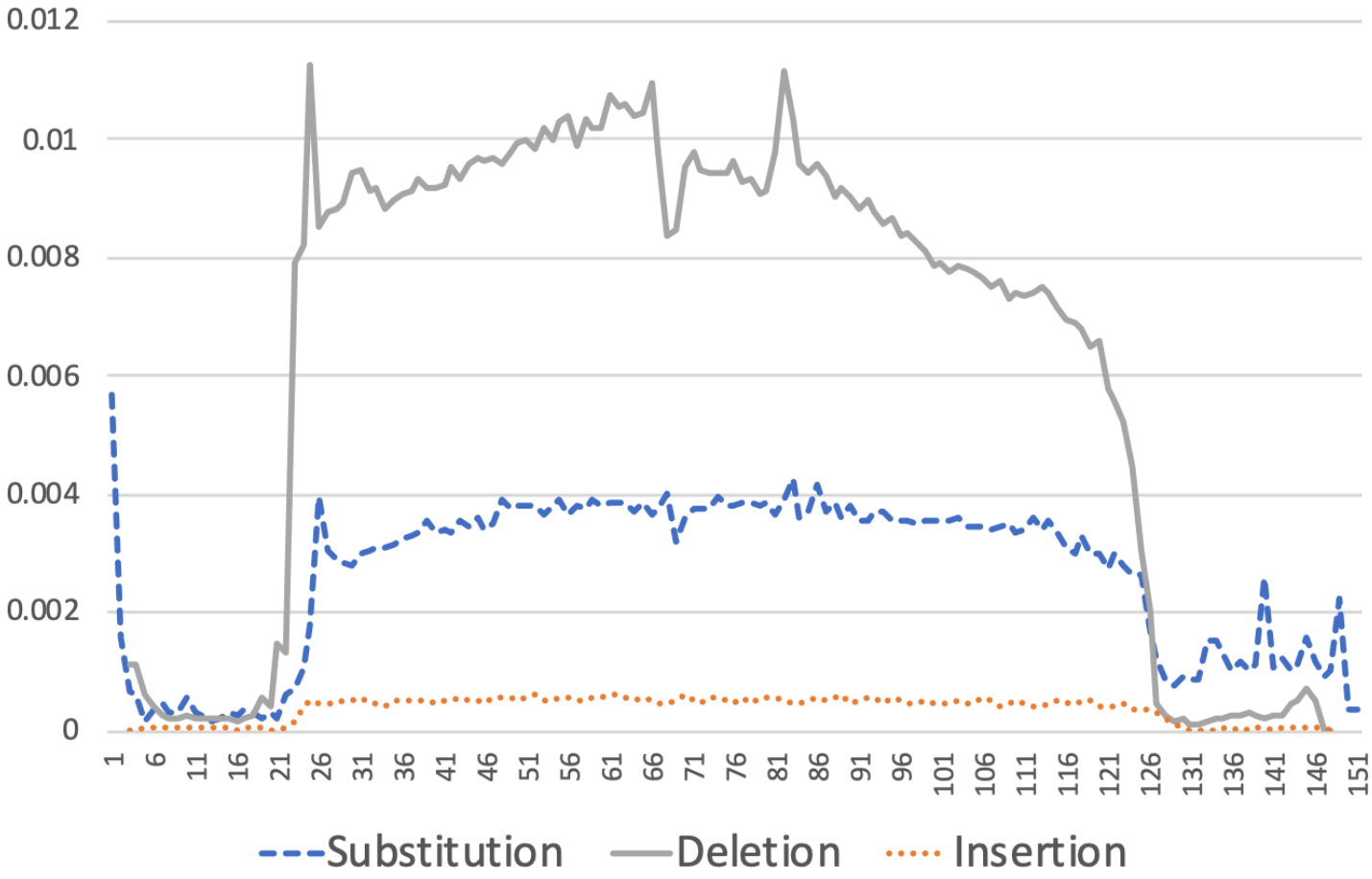
Backup

We first compute the optimal tradeoff between c_w and c_r when $\epsilon = 0$, i.e., the reads are error-free. In this case, for large enough n, we can use the Poisson(λ) approximation for the number of times each sequence is observed with $\lambda = c_r/c_w$. Since the probability of seeing zero copies of a sequence is $e^{-\lambda}$, this gives us an erasure channel with capacity $1 - e^{-\lambda}$ [20]. For reliable recovery, we need that the rate $1/c_w$ be less than the capacity. This gives us

$$c_r \geq c_w \log_e \frac{c_w}{c_w - 1}$$

$$P((k_0, k_1) \mid 0) = \frac{e^{-\lambda}\lambda^{k_0+k_1}}{(k_0+k_1)!}\binom{k_0+k_1}{k_0}(1-\epsilon)^{k_0}\epsilon^{k_1}$$

$$LLR(k_0, k_1) = \ln \frac{P((k_0, k_1) \mid 0)}{P((k_0, k_1) \mid 1)} = (k_0 - k_1) \ln \frac{1-\epsilon}{\epsilon}$$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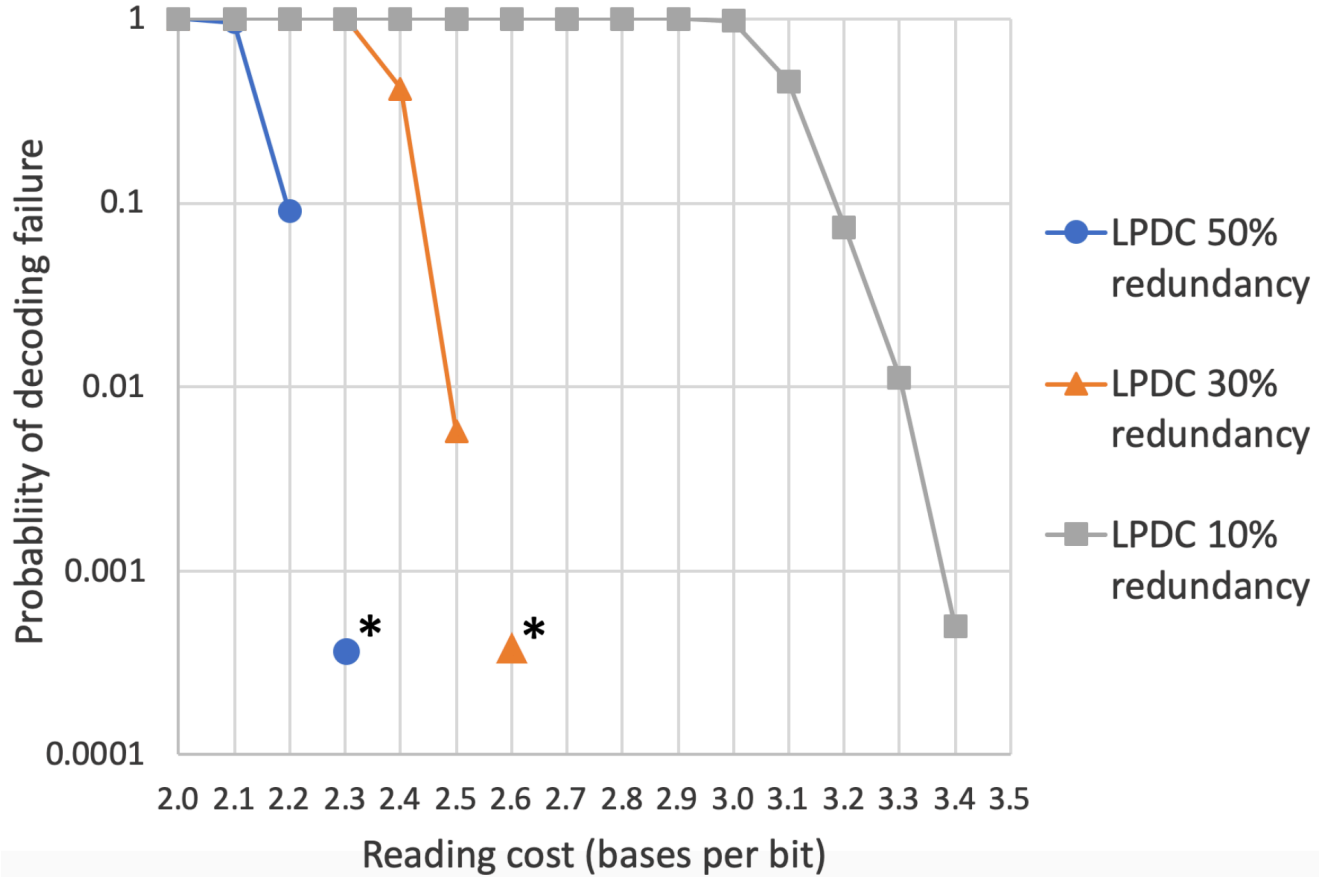
Substitution
Deletion
Insertion


1
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Probablility of decoding failure
2.0 2.1 2.2 2.3 2.4 2.5 2.6 2.7 2.8 2.9 3.0 3.1 3.2 3.3 3.4 3.5
Reading cost (bases per bit)
*
*
LPDC 50% redundancy
LPDC 30% redundancy
LPDC 10% redundancy