Stanford

Error Correcting Codes for DNA based Data Storage

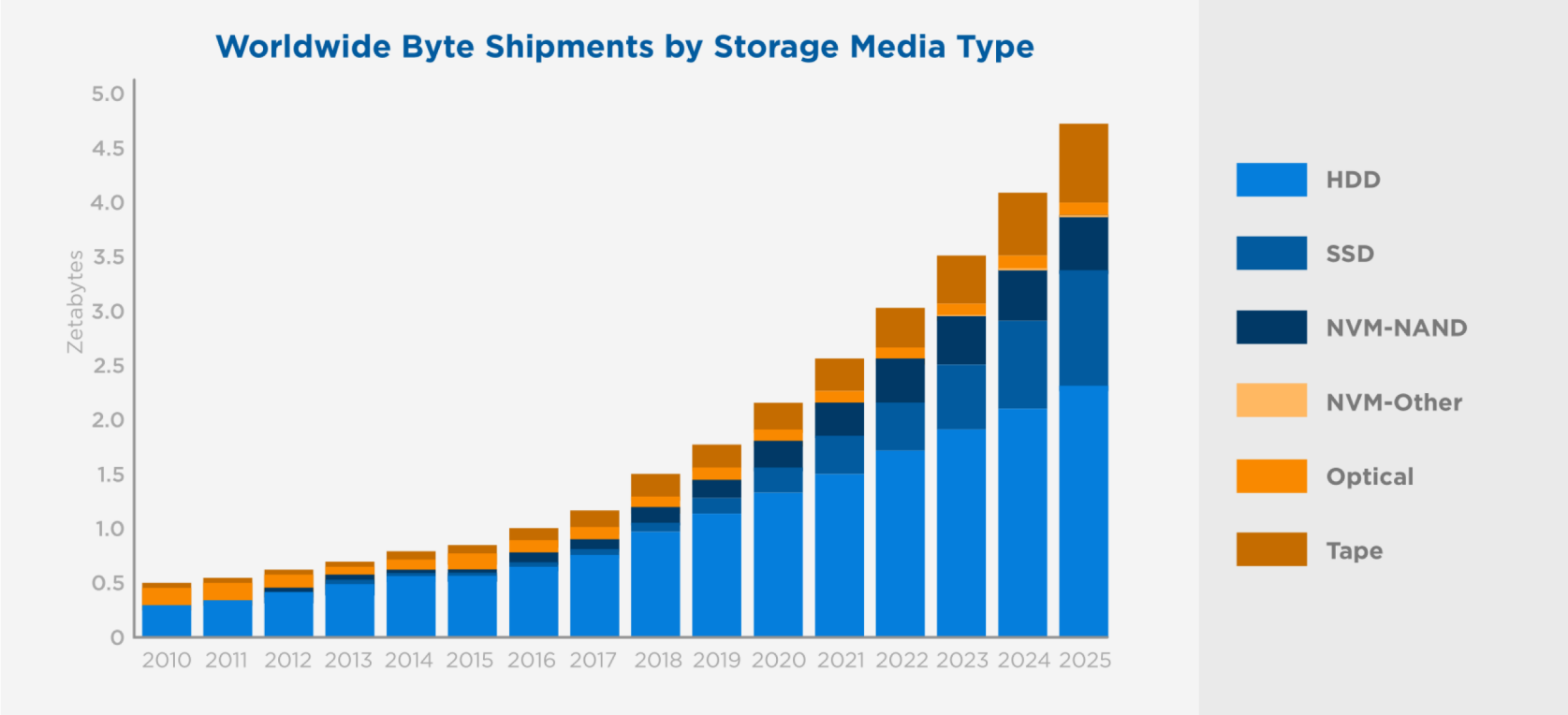
Shubham Chandak
Stanford University
ISMB/ECCB 2019

Outline

- Motivation
- DNA storage setup
- Illumina sequencing-based DNA storage
- Nanopore sequencing-based DNA storage
- 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

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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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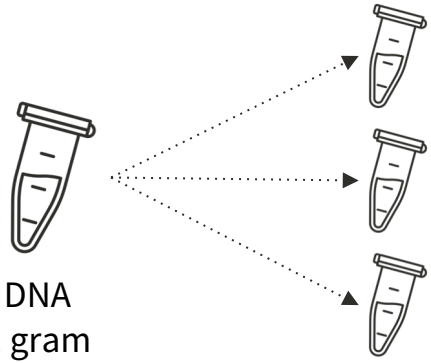

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1,000s of years

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/

How to store data in DNA sequences?

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- Ability to synthesize short ssDNA oligonucleotides (~150 nt) at scale.

CustomArray | GenScript Make Research Easy http://www.customarrayinc.com/

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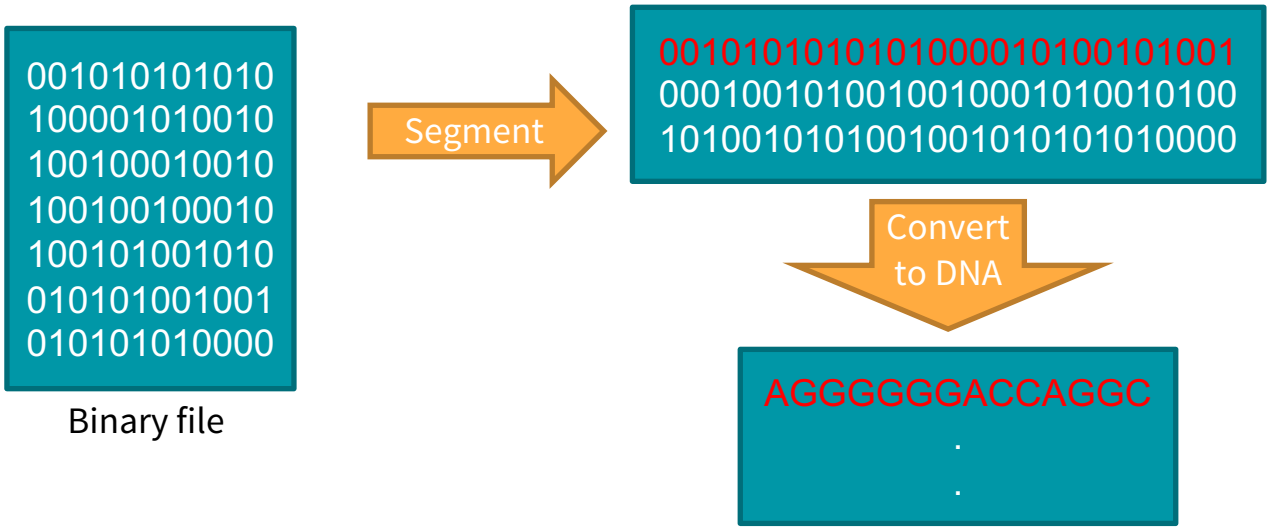

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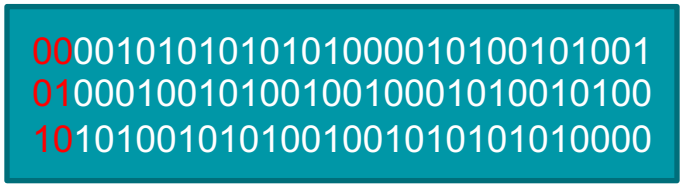

Length of index in binary segment at least $\log_2$(number of segments)

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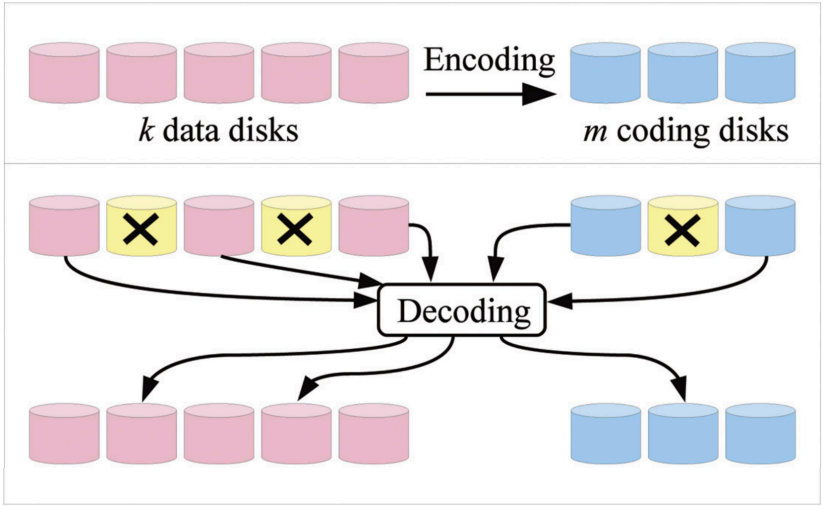

Also used in traditional storage systems (e.g., RAID)

Figure source: https://www.usenix.org/system/files/login/articles/10_plank-online.pdf

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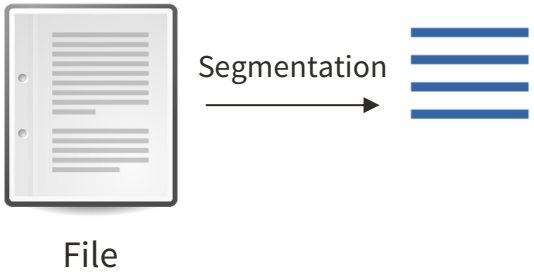
Error/Erasure Correcting Codes enable reliable data recovery even for noisy, low cost synthesis and sequencing – likely to be the future of DNA storage.

DNA storage setup

Typical DNA Storage System

File

Typical DNA Storage System



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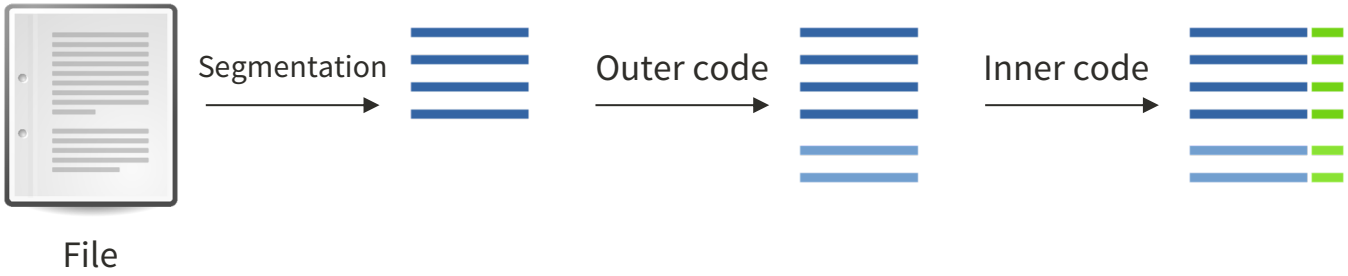

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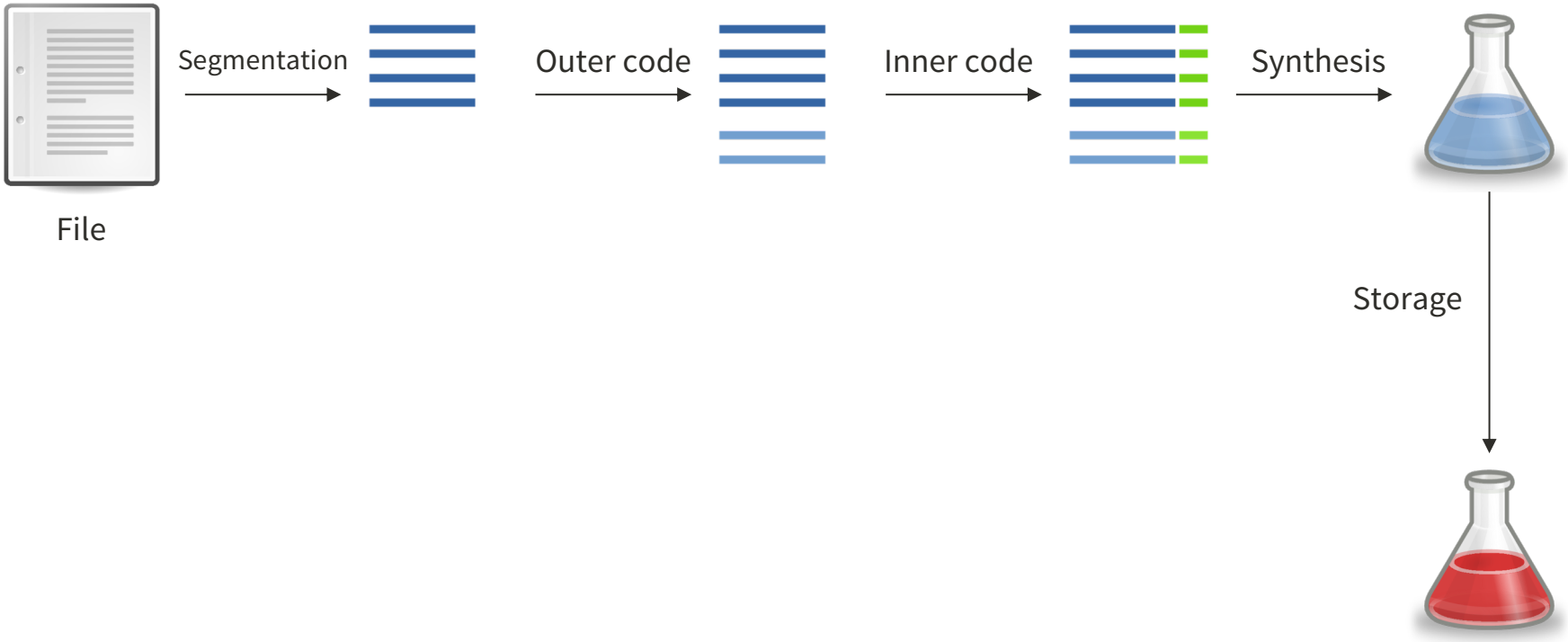

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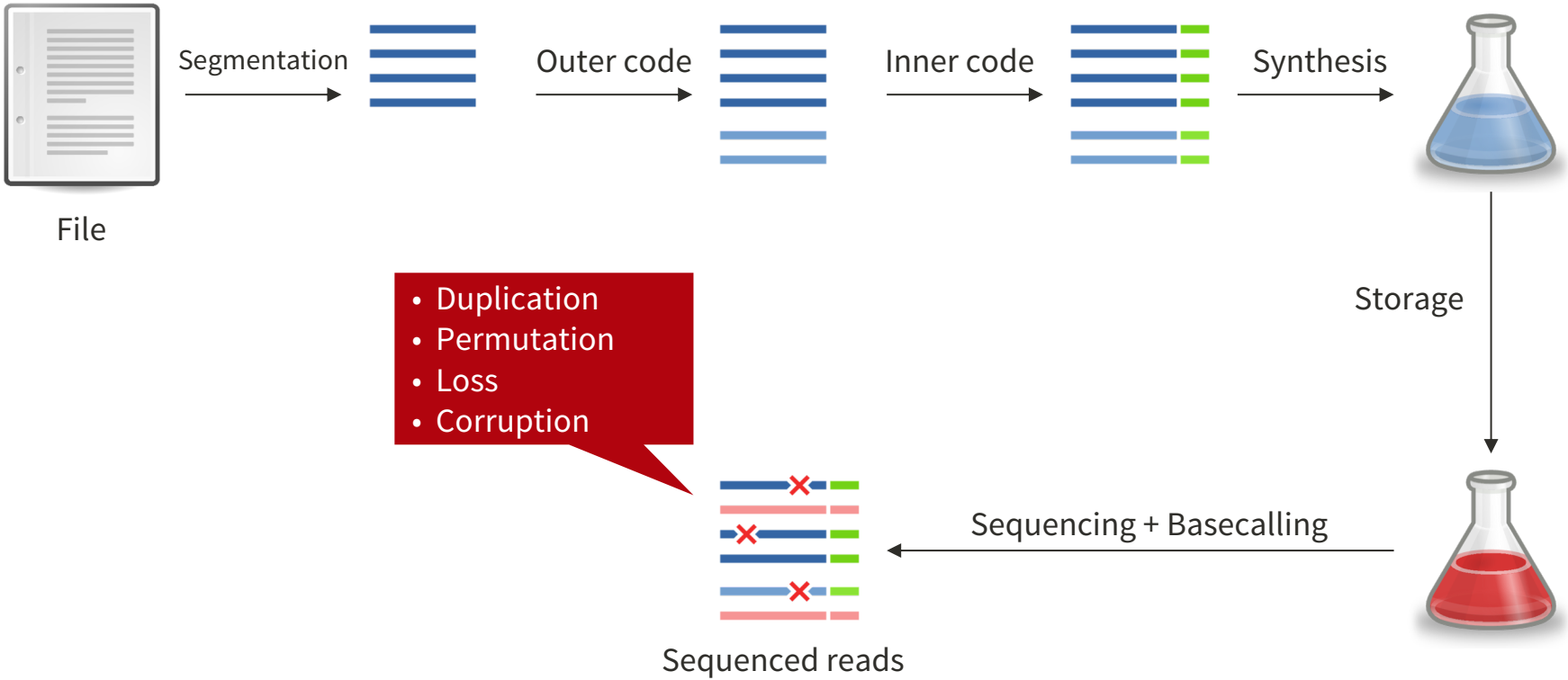

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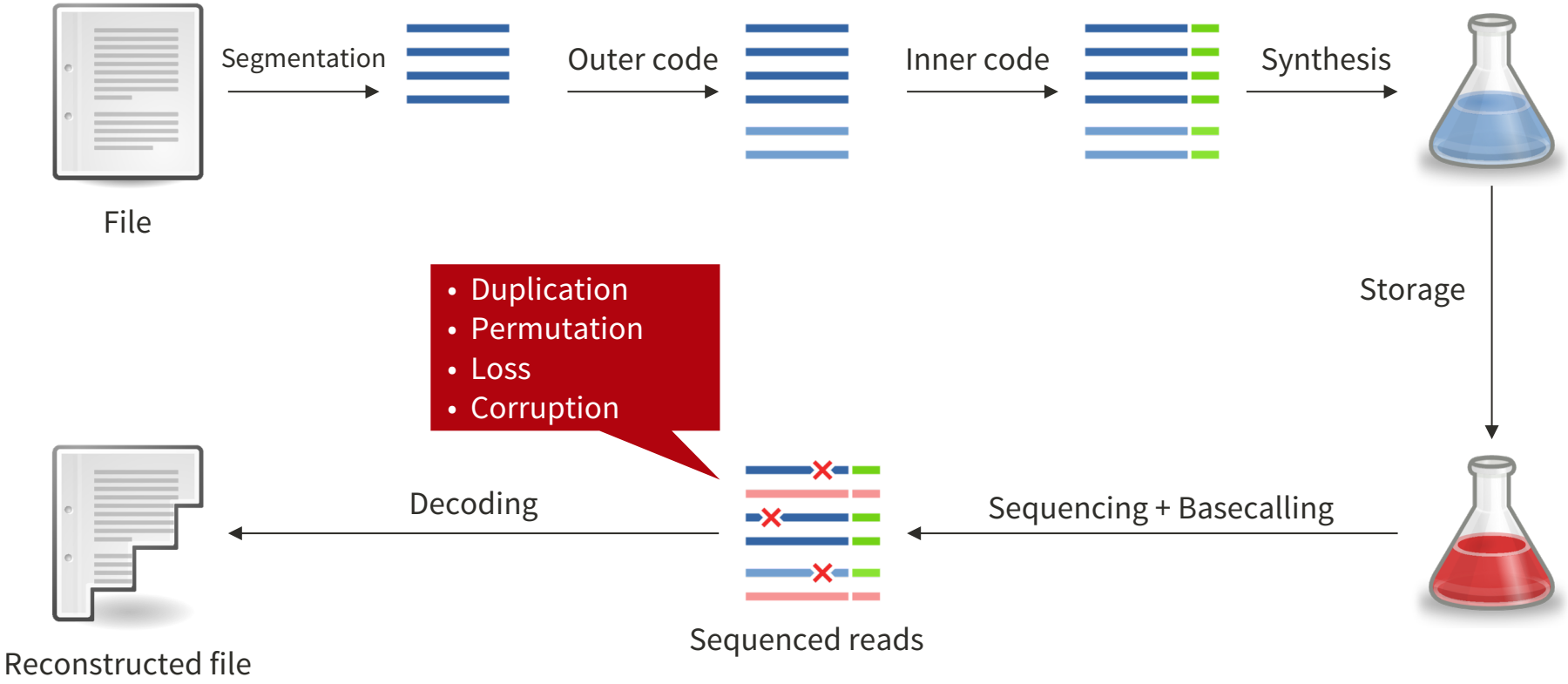

2nd gen sequencing

Illumina sequencing

Portability	❌
Real-time	❌
Long reads	❌
Throughput	✅
Error rates	**< 1%**

{ mostly substitutions

3rd gen sequencing

Nanopore sequencing

Portability	✅
Real-time	✅
Long reads	✅
Throughput	❌
Error rates	**10 - 15%**

{ insertions, deletions, substitutions

Previous works

- Multiple previous works focusing on:
  - Error correction coding
  - Random access of subsets of 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.

Our contribution

- Fundamental quantities to evaluate a DNA storage system:
  - Writing cost (bases synthesized/message bit)
  - Reading cost (bases sequenced/message bit) (*not* coverage)

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- Basecaller-decoder integration for nanopore to exploit additional information in raw current signal.

Illumina sequencing-based DNA storage

Key idea

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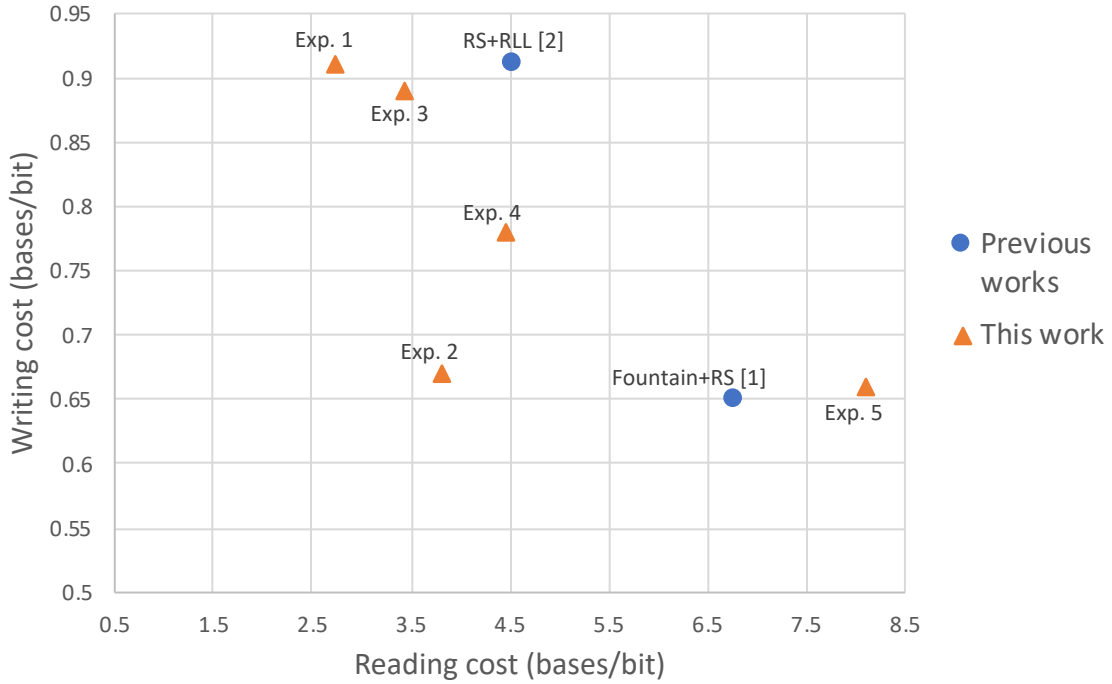
✗ Strategy 1: Inner/outer code separation

✓ Strategy 2: Single large block code (LDPC)

Experimental Results

- 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.
- Approach combines LDPC codes with heuristics for handling deletion errors.

Experimental Results



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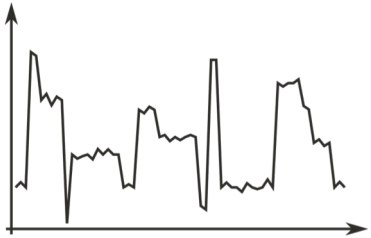
Nanopore sequencing-based DNA storage

Nanopore Sequencing Model

… ACGTACGTACGT …

Nanopore sequencing channel

- Memory (inter-symbol interference)
- Base skips
- Fading
- Random symbol duration
- Noise



Source: "Models and Information-Theoretic Bounds for Nanopore Sequencing", Wei Mao et al., IEEE Trans. Inf. Theory 2017

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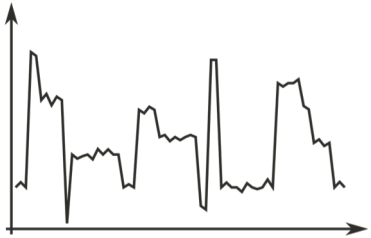

VERY HARD TO MODEL AND ANALYZE FAITHFULLY

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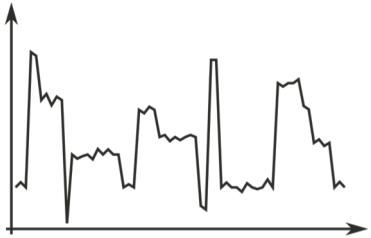

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COMBINE STRENGTHS OF MACHINE LEARNING & CODING THEORY!

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Our approach

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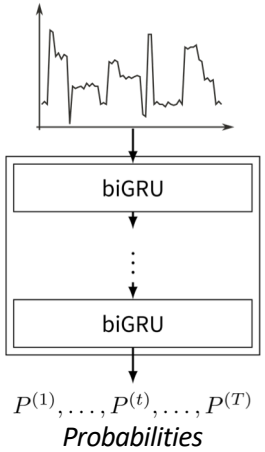
Using Flappie basecaller (Oxford Nanopore)



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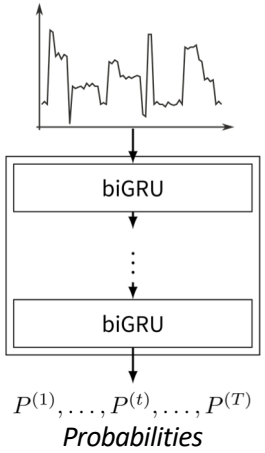

Basecalling
Code constraints not used

AACGT ✗

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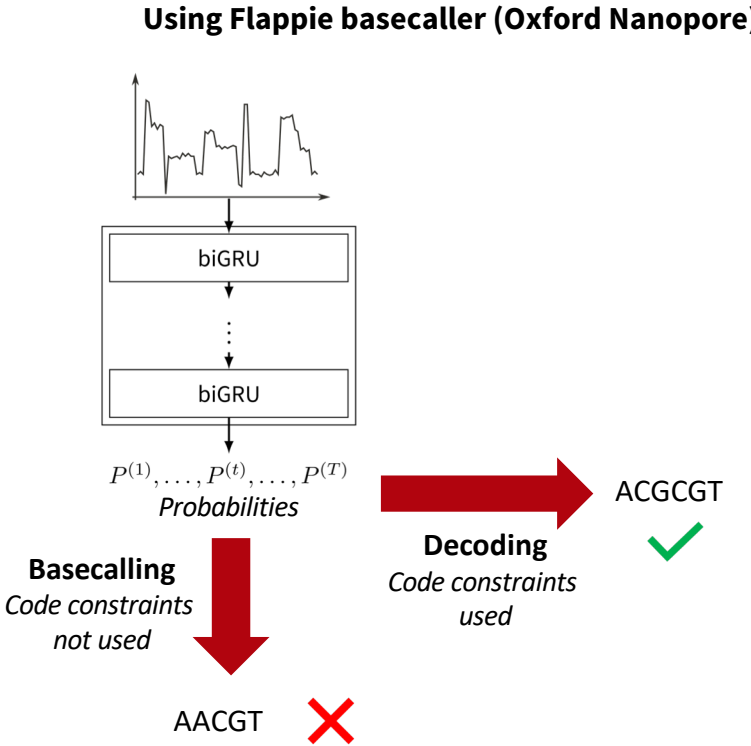

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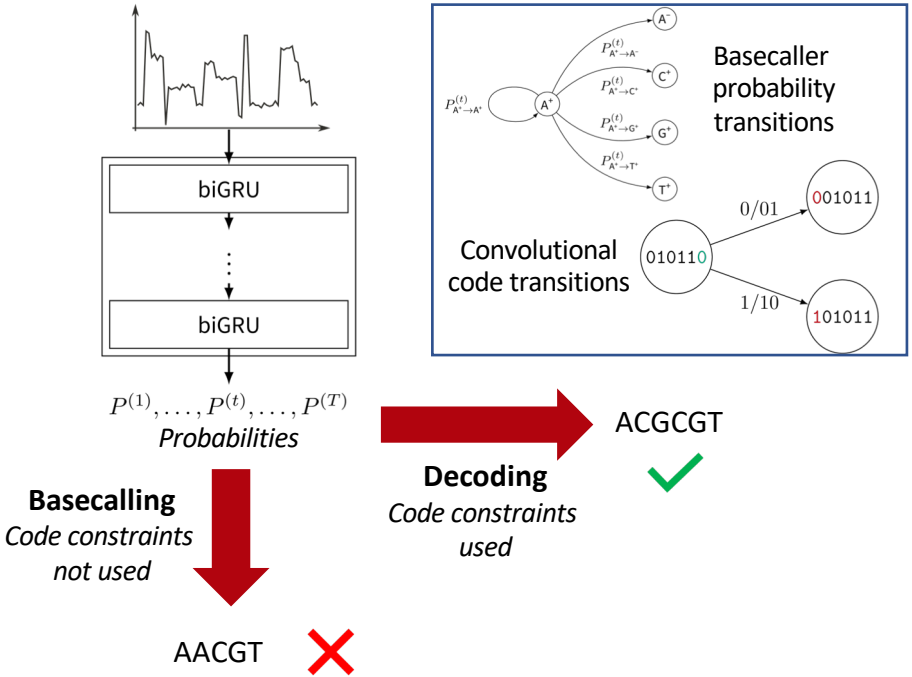

Preliminary Results

- Around **3x-6x** lower reading costs than state-of-the-art [1].

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Preliminary Results

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- Suggests that **raw signal** carries much **more information** than **basecalled sequence** - this can help other bioinformatics applications as well.

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Conclusions and future work

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- Plan to integrate these with random access and repeated reading.
- Long term vision: Nanopore sequencing + cheaper and noisier synthesis techniques:
    - Basecaller-decoder integration works with various synthesis strategies, e.g., k-mer by k-mer
- Core idea behind basecaller-decoder integration applicable beyond DNA storage:
    - Bioinformatics (soft-information based processing) - e.g., nanopolish
    - Communication (coding for complex and hard-to-model channels)

Team and funding

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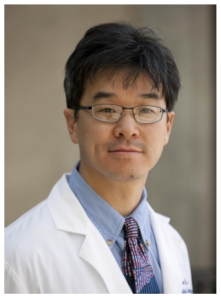

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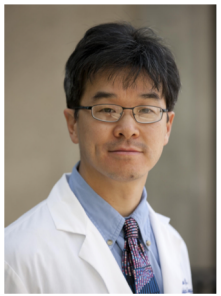


Hanlee Ji

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

Beckman Center Innovative Technology Seed Grant

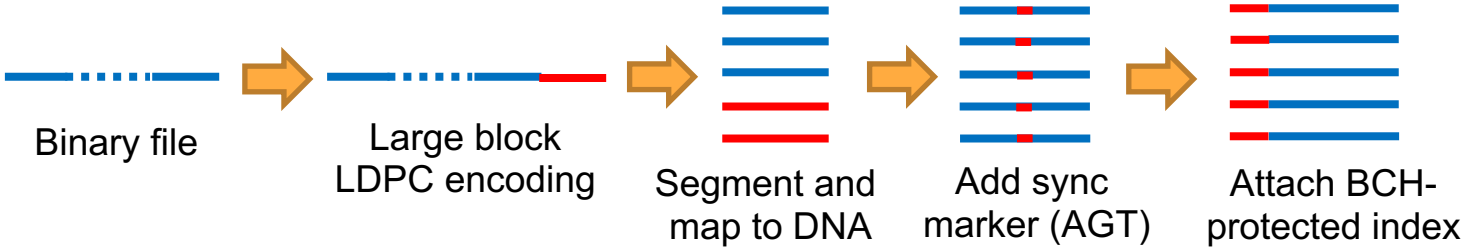
Scalable Long-Term DNA Storage with Error Correction and Random-Access Retrieval

National Institutes of Health

Thank You

Poster session today 6pm-8pm: V-071

Proposed approach - schematics



Encoding

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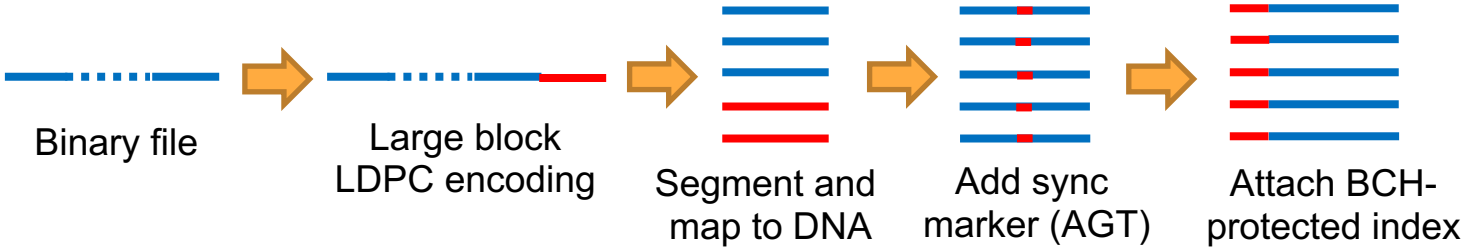

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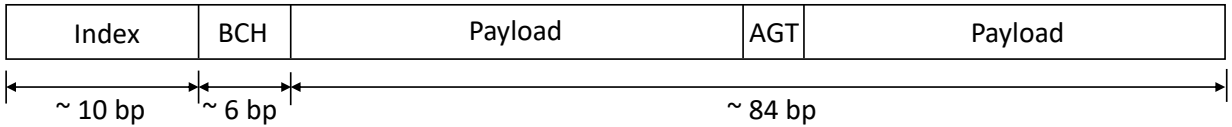

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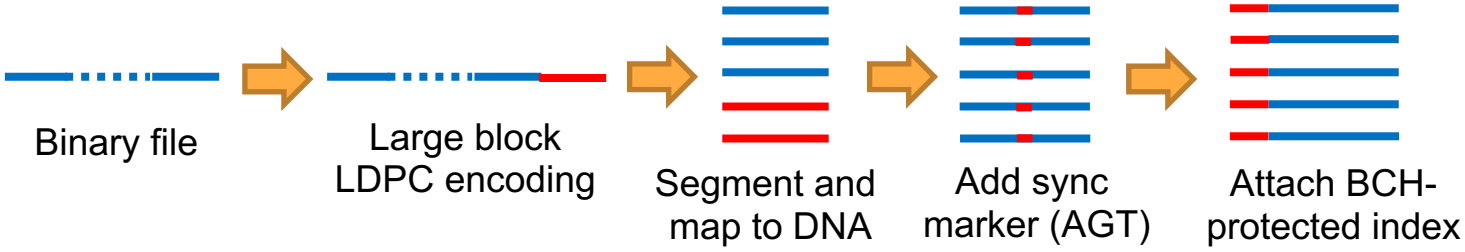

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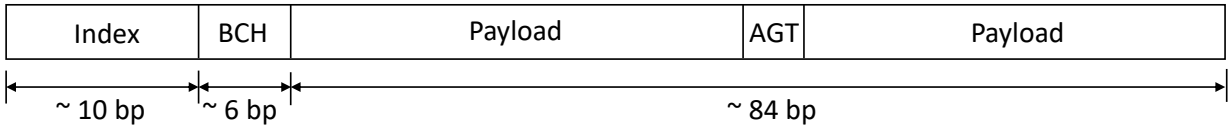
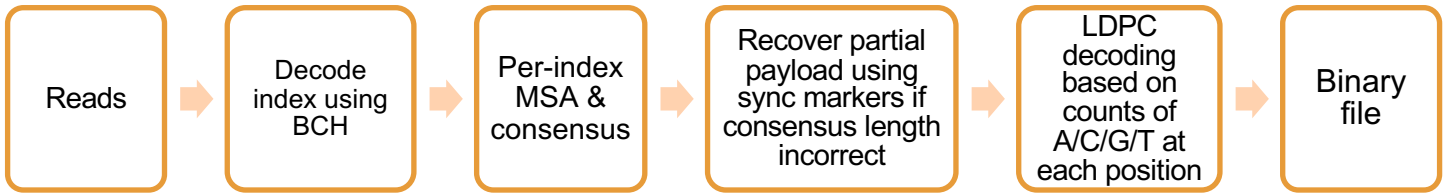
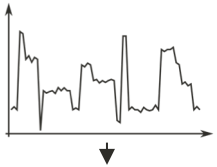




Decoding

Our approach

Stanford



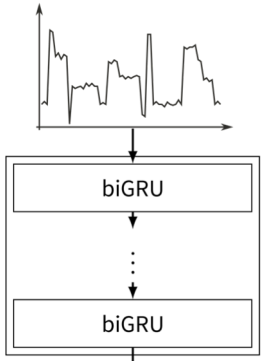
Deep neural network (DNN) basecaller (state-of-the-art)

Soft information

Viterbi convolutional decoder

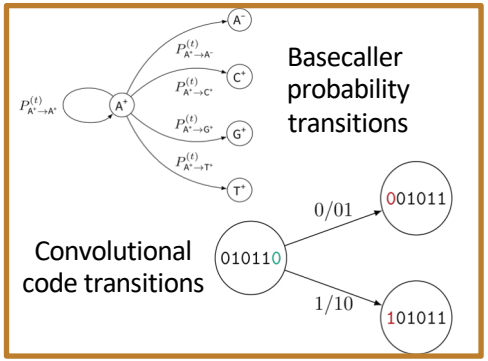
10111 …
10011 …
10101 …

Using Flappie basecaller (Oxford Nanopore)



$P^{(1)}, \ldots, P^{(t)}, \ldots, P^{(T)}$

Probabilities



Basecalling
Code constraints not used

AACGT ✗

Decoding
Code constraints used

ACGCGT ✓