Stanford

Overcoming high nanopore basecaller error rates for DNA storage via basecaller-decoder integration and convolutional codes

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ICASSP 2020

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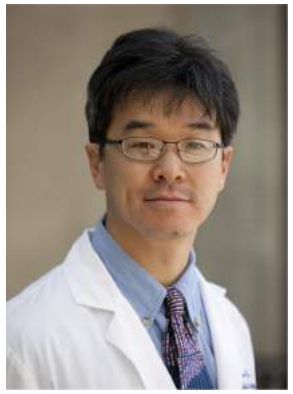

Hanlee Ji

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

Beckman Center Innovative Technology Seed Grant

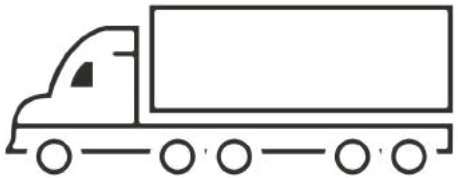
Scalable Long-Term DNA Storage with Error Correction and Random-Access Retrieval

National Institutes of Health

Motivation

200 Petabyte

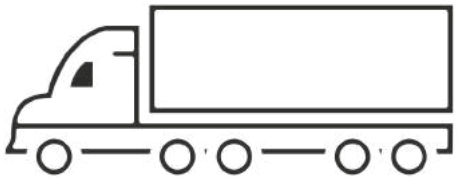
200 Petabyte



40,000 x 5 TByte HDDs
40 tons

10s of years

200 Petabyte



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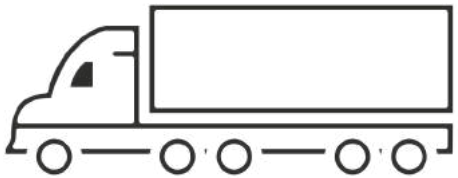
DNA
1 gram

1,000s of years

200 Petabyte



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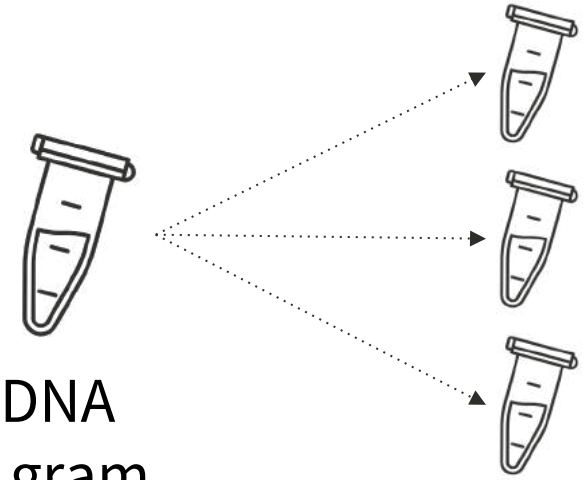


DNA
1 gram

Easy duplication

1,000s of years

DNA storage setup

Building block: synthesis

- Ability to “**write/synthesize**” artificial DNA (sequence of {A,C,G,T})

CustomArray | GenScript Make Research Easy

Current ability: short ssDNA oligos (~150nt) at scale

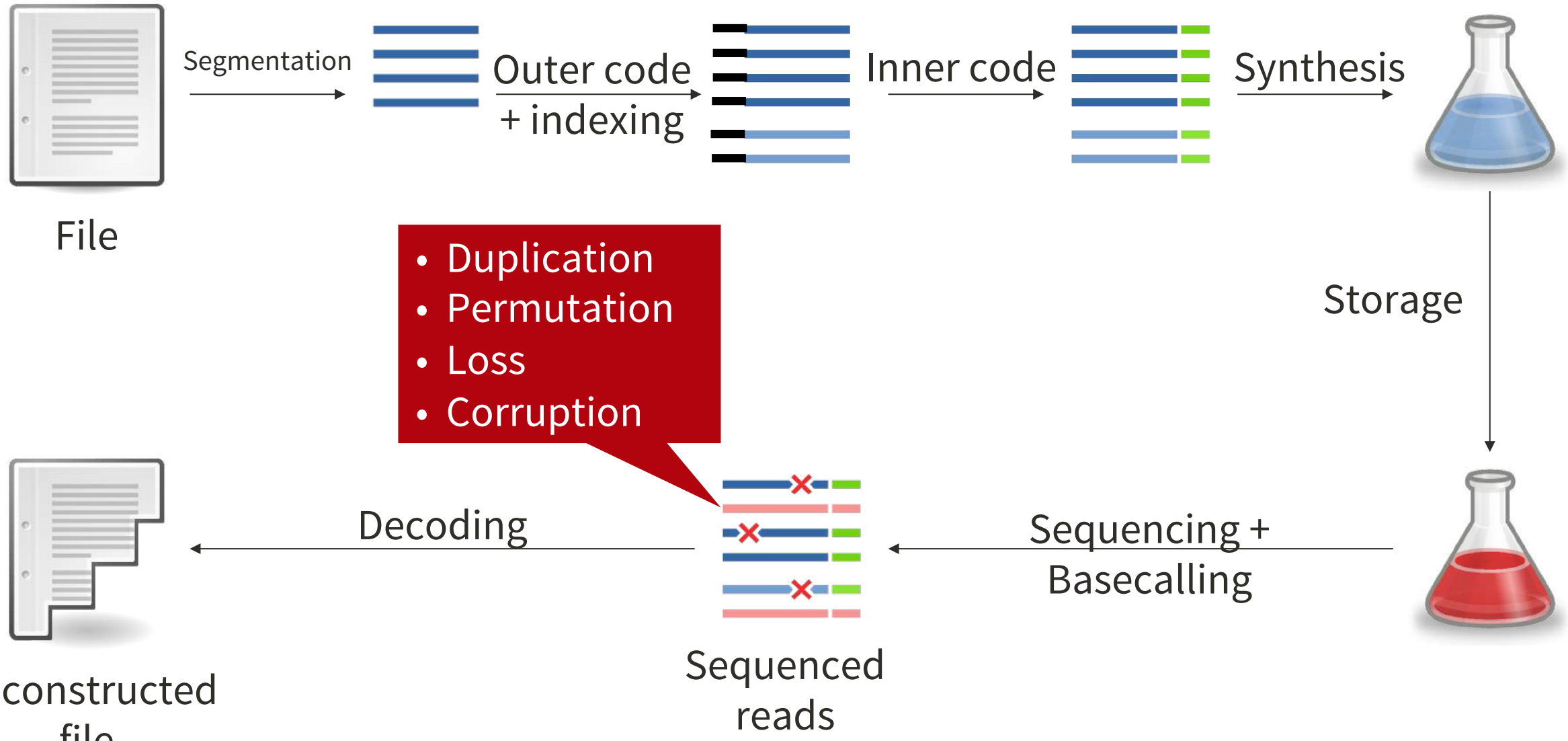
DNA Synthesis is not perfect: Usually has ~1% insertion/Deletion error

Building block: sequencing

- Nanopore sequencing: portable, real time

https://directorsblog.nih.gov/2018/02/06/sequencing-human-genome-with-pocket-sized-nanopore-device/

Typical DNA Storage System



Challenges

- High basecall error rates for nanopore sequencing
  - 5-10% edit distance
  - Predominantly insertion and deletion errors
- Lack of good error correction codes for this setting

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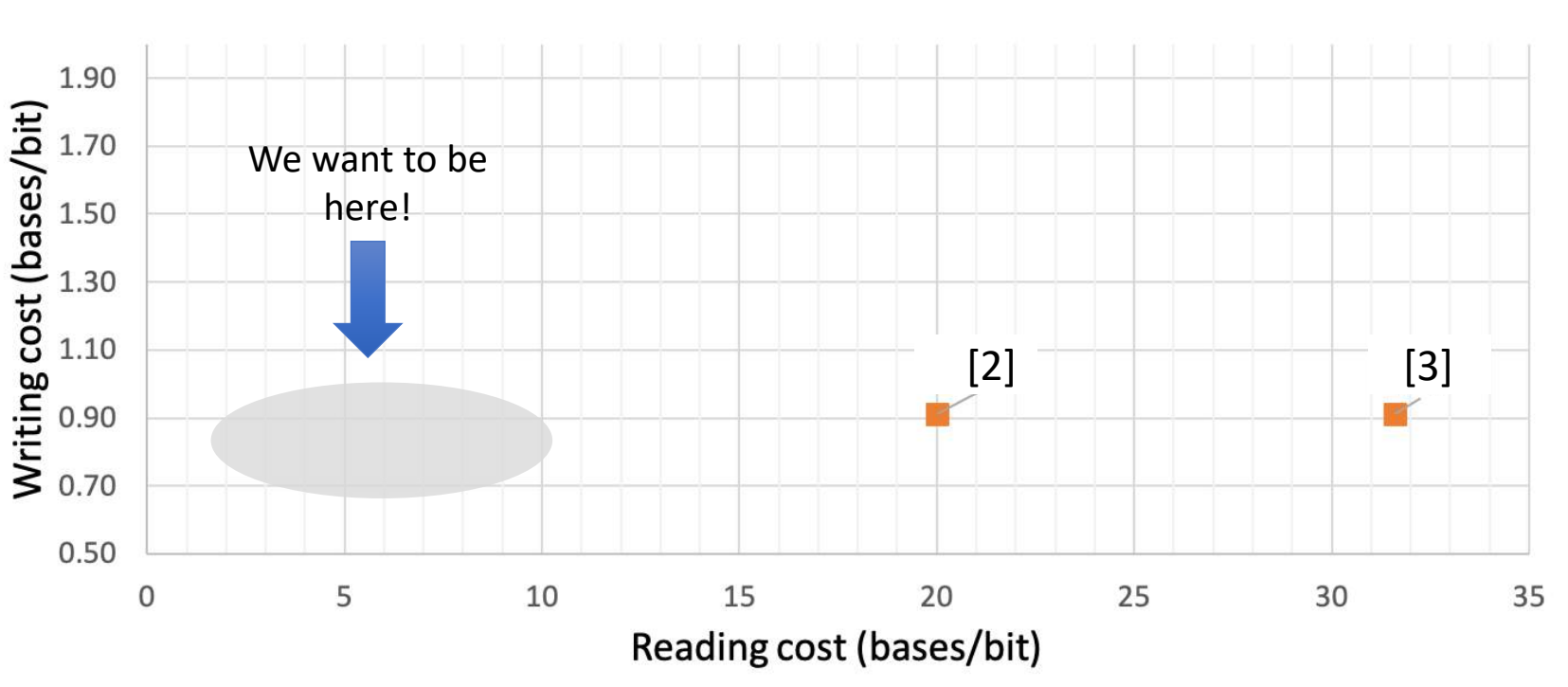
- High basecall error rates for nanopore sequencing
  - 5-10% edit distance
  - Predominantly insertion and deletion errors
- Lack of good error correction codes for this setting
- Most previous works rely on consensus over multiple reads – **high reading cost**
  - Sequence the input lot of times (~30-40x)
  - Cluster by *index*, and perform “averaging” to reduce the error

Previous Works

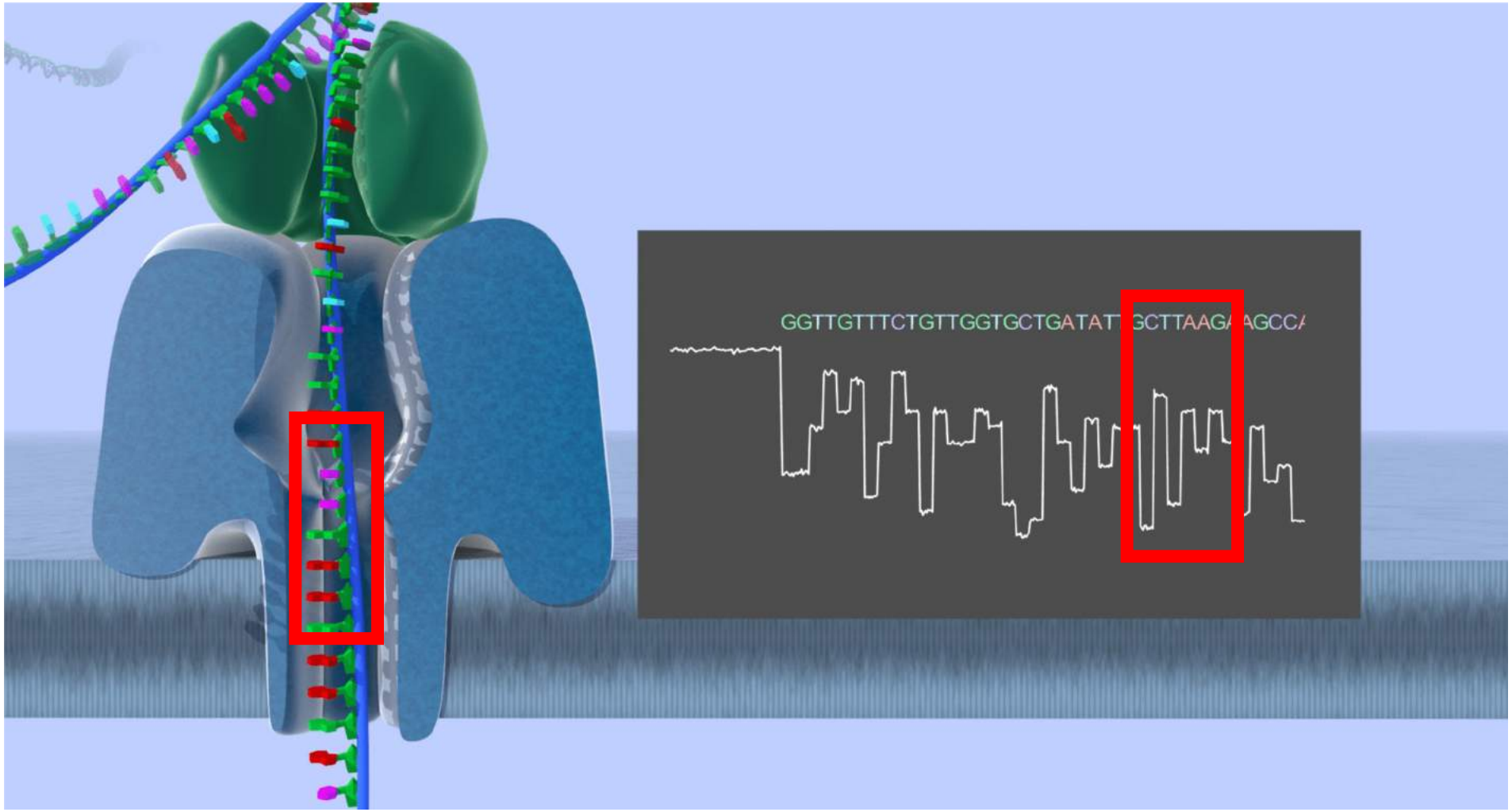


[2] L. Organick *et al.*, “Random access in large-scale DNA data storage," *Nature biotechnology*, vol. 36, no. 3, p. 242, 2018.

[3] Randolph Lopez et al., “DNA assembly for nanopore data storage readout,” Nature communications, vol. 10, no. 1, pp. 2933, 2019.

Methods

Nanopore Physics

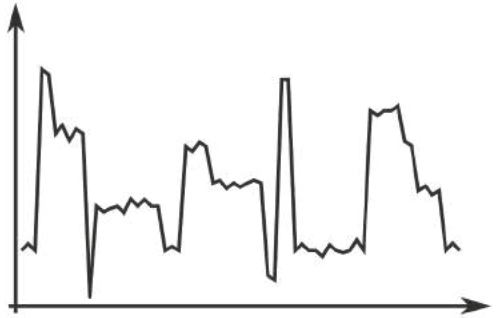


Nanopore Sequencing Model

… 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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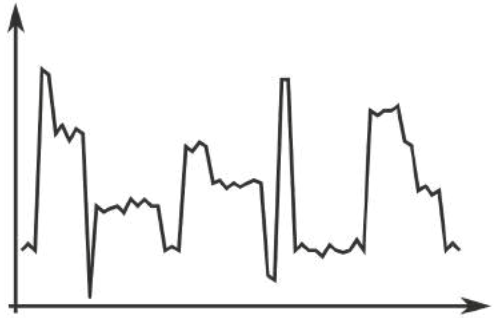

VERY HARD TO MODEL AND ANALYZE FAITHFULLY

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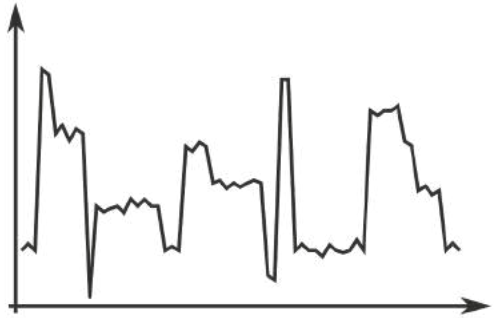

VERY HARD TO MODEL AND ANALYZE FAITHFULLY

COMBINE STRENGTHS OF MACHINE LEARNING & CODING THEORY!

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

Key idea

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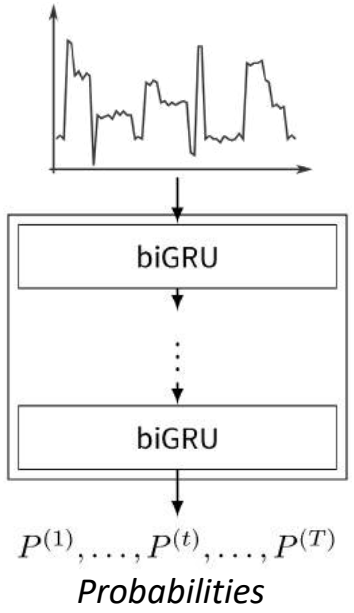
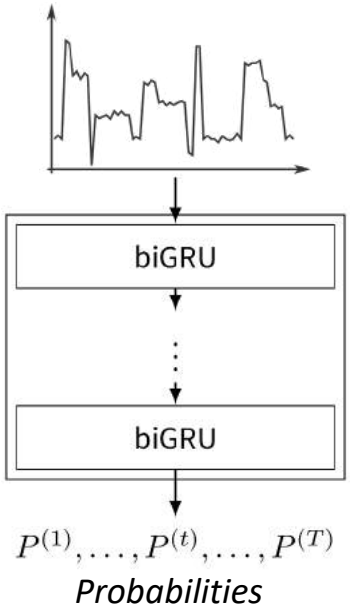


Using Flappie basecaller (Oxford Nanopore)

Key idea

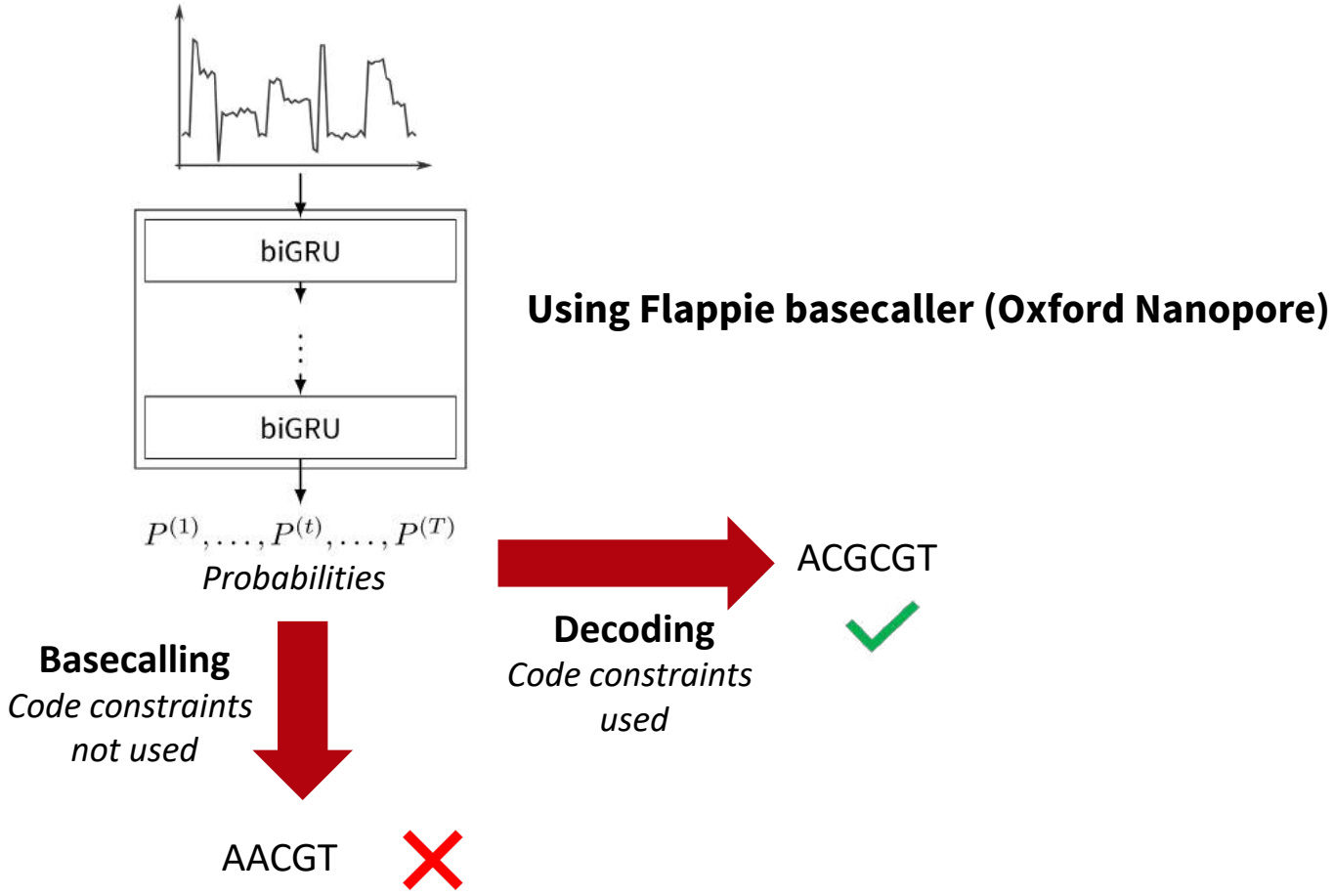


Basecalling
Code constraints not used

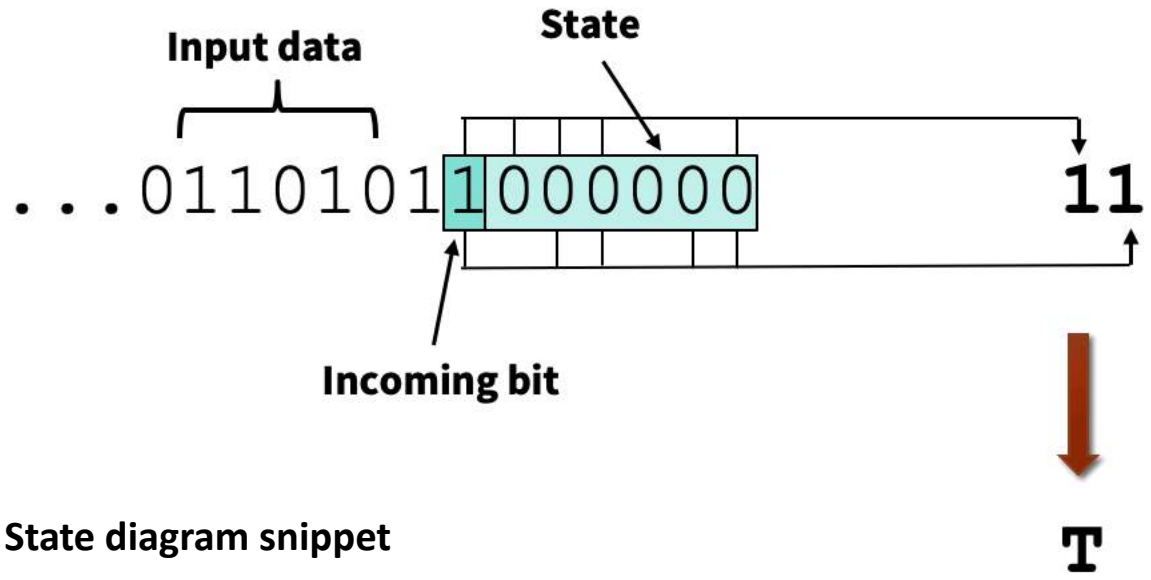
AACGT ✗

Using Flappie basecaller (Oxford Nanopore)

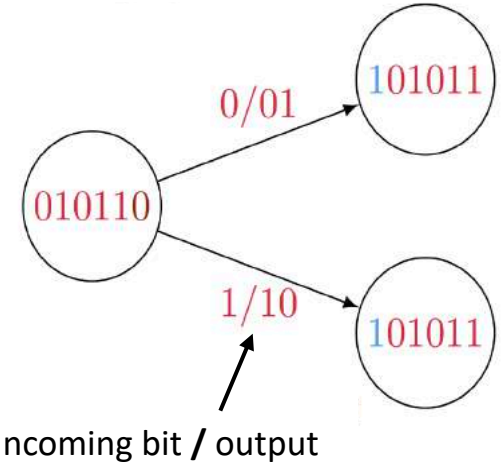
Key idea


biGRU
biGRU
$P^{(1)}, \ldots, P^{(t)}, \ldots, P^{(T)}$
Probabilities
Using Flappie basecaller (Oxford Nanopore)
Decoding
Code constraints used
ACGCGT
Basecalling
Code constraints not used
AACGT

Convolutional Codes as the Inner Code



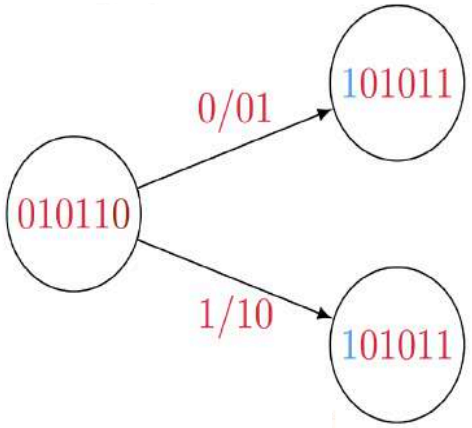
State diagram snippet



Convolution code parameters:
r = 1/2 (rate)
m = 6 (memory)

Basecaller-decoder integration

Convolutional code



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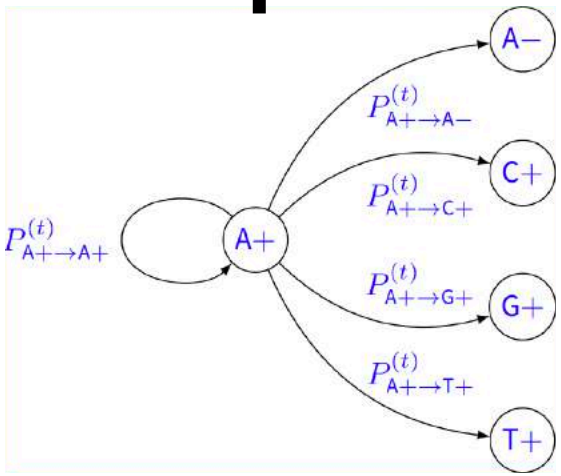
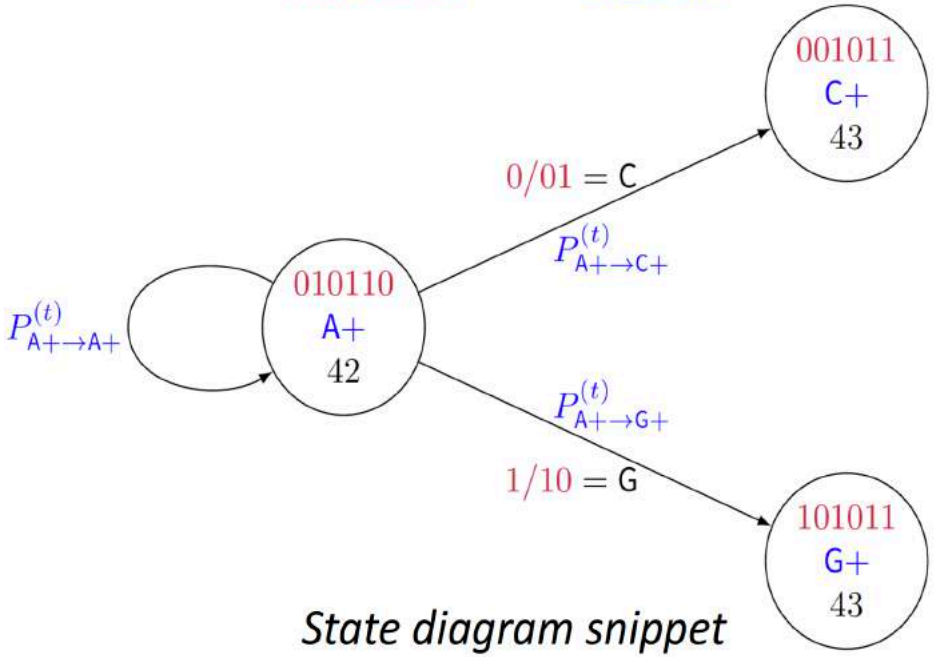


NN-modeling based transition probabilities

=

Combining NN-modeling + convolutional codes

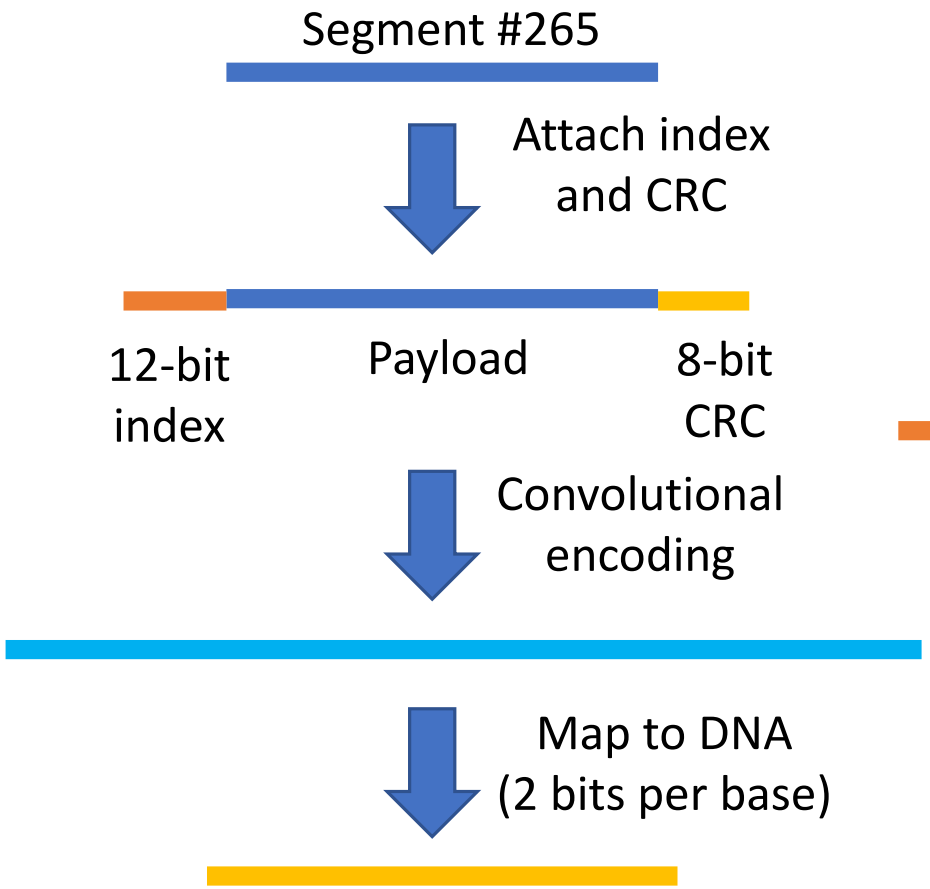
state = (state$_{convolutional}$, state$_{basecaller}$, position)



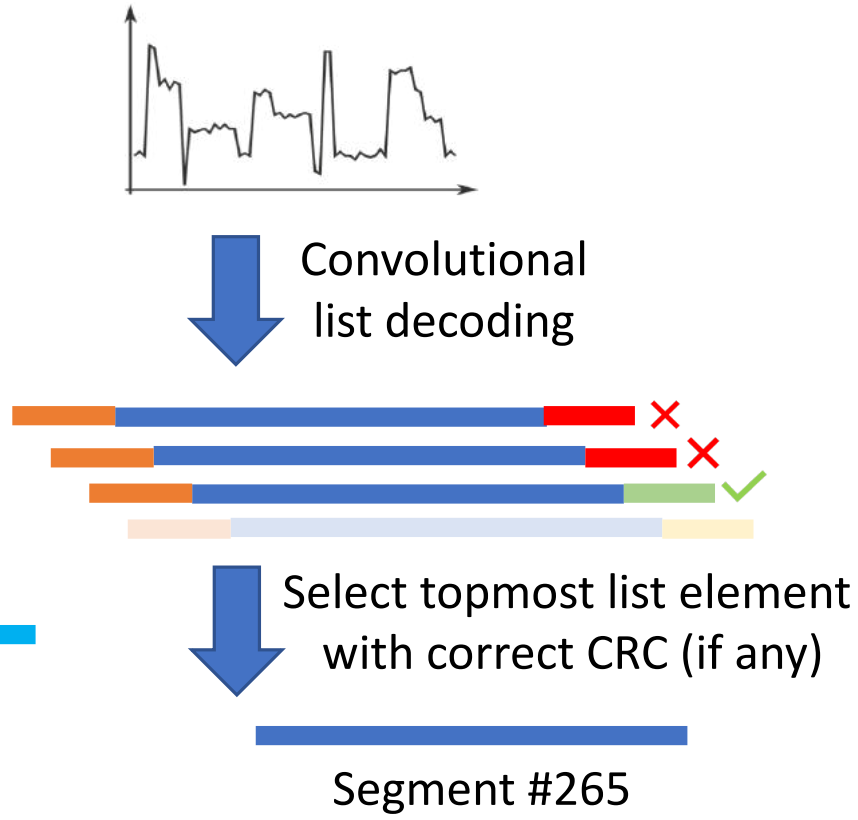
State diagram snippet

Perform Viterbi decoding using the modified state diagram

Overall Inner Code design



(a) Inner code encoding



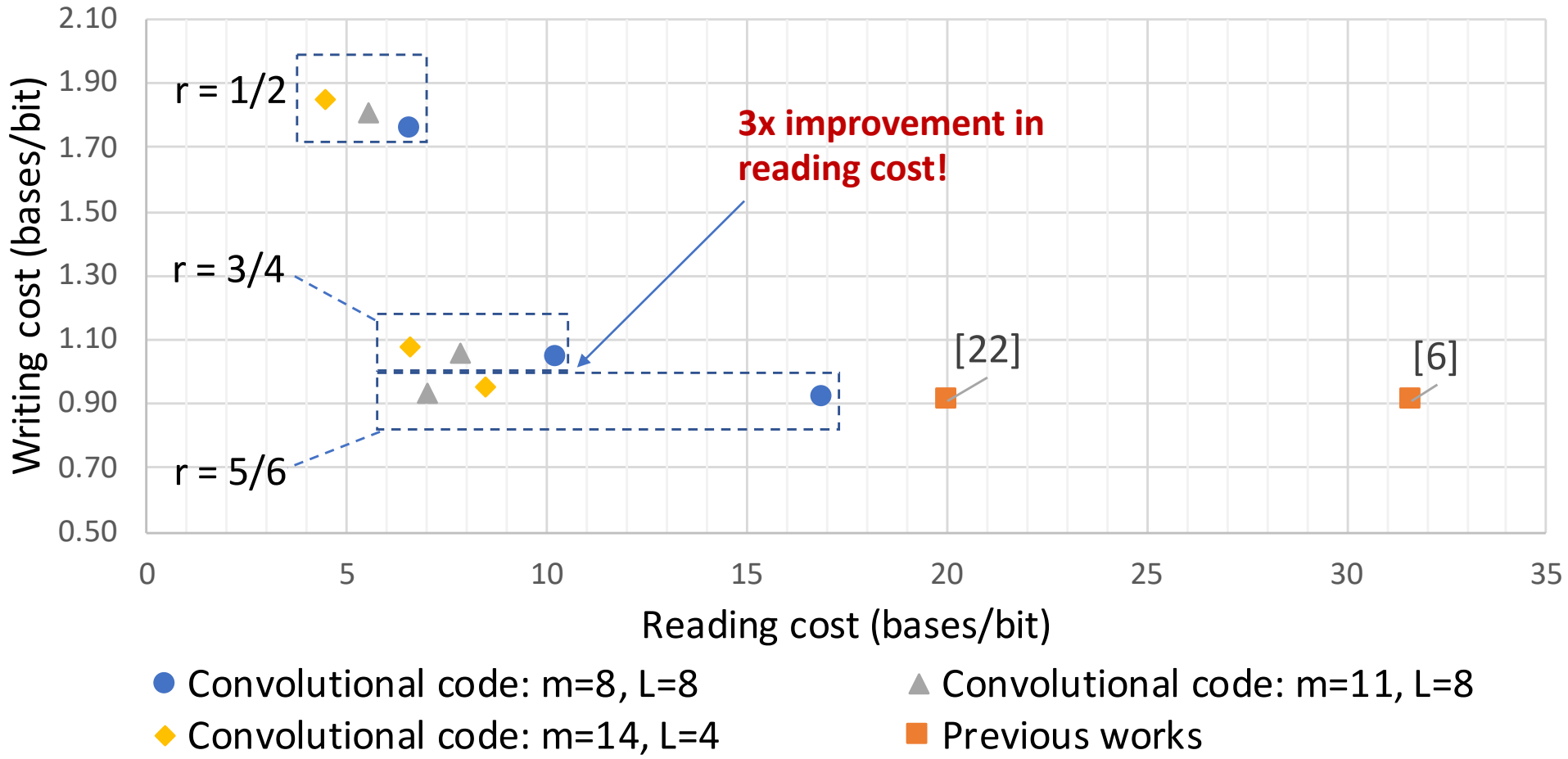
(b) Inner code decoding

Experiments and results

Experiments

- **Data**: 11KB of data: The Gettysburg Address, UN Declaration, “I have a Dream” Speech, poem collections, …
- **Final Error Correction Code Design:**
  - Reed Solomon outer code: 30% redundancy (default)
  - Pretrained Model from the ONT Flappie Basecaller
- **Synthesis:** Data Synthesized using CustomArray synthesis, into oligos of length ~165
- **Experiments:**
  - Rate of convolution code: r = 1/2, 3/4, 5/6
  - Memory: m = 8,11,14
  - List Size: 4, 8

Results



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Conclusions and future work

- Novel error-correction mechanism for nanopore sequencing based DNA storage
  - Use “soft-information” from raw signal to improve decoding
  - Use neural net in basecaller to distil information from “hard-to-model” raw signal
  - Use convolutional codes that align nicely with sequential nanopore model
- Requires 3x fewer reads for decoding than previous works

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  - Use convolutional codes that align nicely with sequential nanopore model
- Requires 3x fewer reads for decoding than previous works
- Future work:
  - Optimization of convolutional code and CRC parameters
  - Finetuning of neural network model and use of improved basecallers
  - Application to other novel synthesis methodologies

Thank You!

Code and data available at

https://github.com/shubhamchandak94/nanopore_dna_storage