ACOMA

Adaptive Codec for Organic Molecular Archives

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Goals

- Provide high bit density
- Adapt to oligos of different lengths
- Adapt to different errors
  - Error types
  - Error rates for different types
  - Spatial distribution of errors
  - Missing whole oligos

DNA Codec Challenges

- Short sequences (at the moment)
- Need for oligo identification
- “Structural” oligo restrictions
  - Homopolymer length
  - CG Content
- Sources of errors
  - Synthesis
  - Amplification
  - Sequencing
- Types of errors
  - Substitutions
  - Deletions
  - Insertions

Bit Packing

- How to encode as many bits as possible per nucleotide (nt)?
- Deal with “structural” errors only
- Theoretical maximum: 2 b/nt
- Existing methods:
  - Goldman et al.: 1.58 b/nt
  - Grass et al.: 1.78 b/nt
  - Erlich et al.: 1.98 b/nt

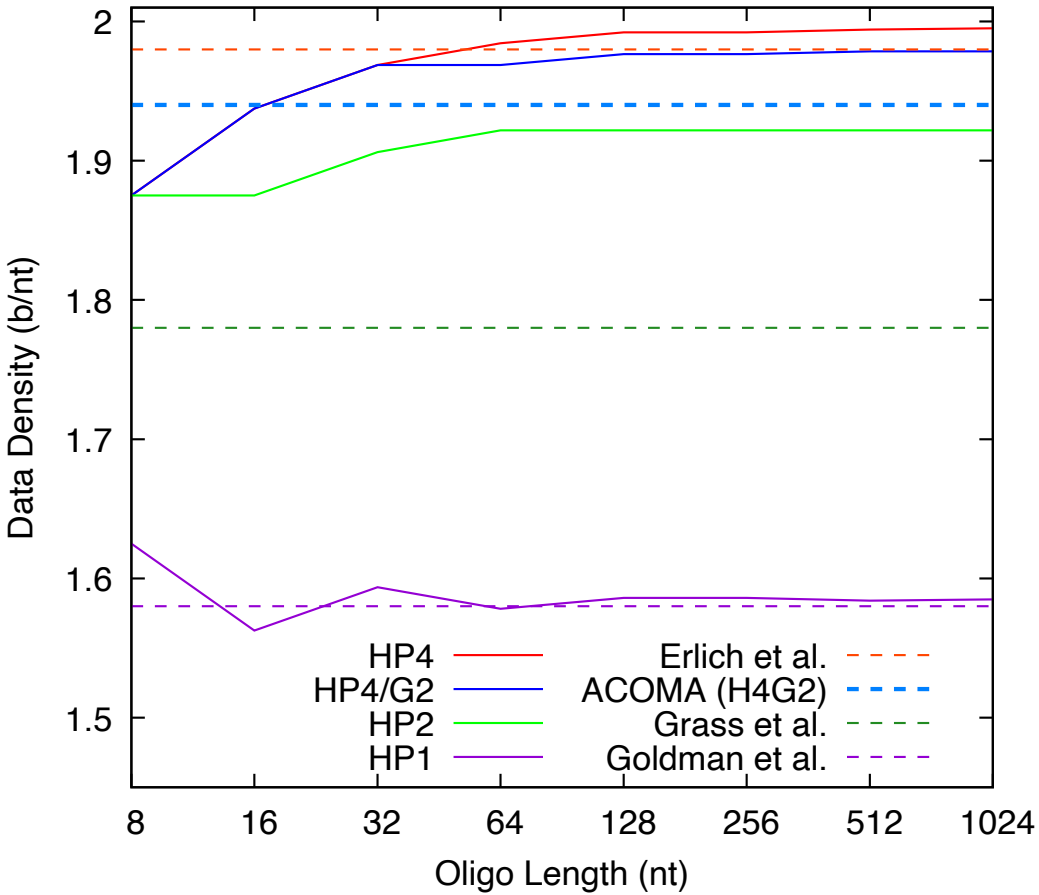
Bit Packing

Oligo counting

- Order oligos
- Reject the ones that fail criteria

~~*AAAAA*~~	~~*X*~~
AAAAT	*0*
AAAAC	*1*
…	
AAGGC	*61*
~~*AAGGG*~~	~~*XX*~~
ATAAA	*62*
…	
GGCGG	*980*
~~*GGGAA*~~	~~*XXX*~~
…	
~~*GGGGG*~~	~~*XXX*~~

Total: 981 values (1.8 b/nt)



ACOMA Codec

- **Level 0**: bit packing
  - How to convert between bits and nts
- **Level 1**: single oligo layout
  - Oligo identification (+ metadata error correction)
  - Data
- **Level 2**: error correction with multiple oligos
  - Error correction for data

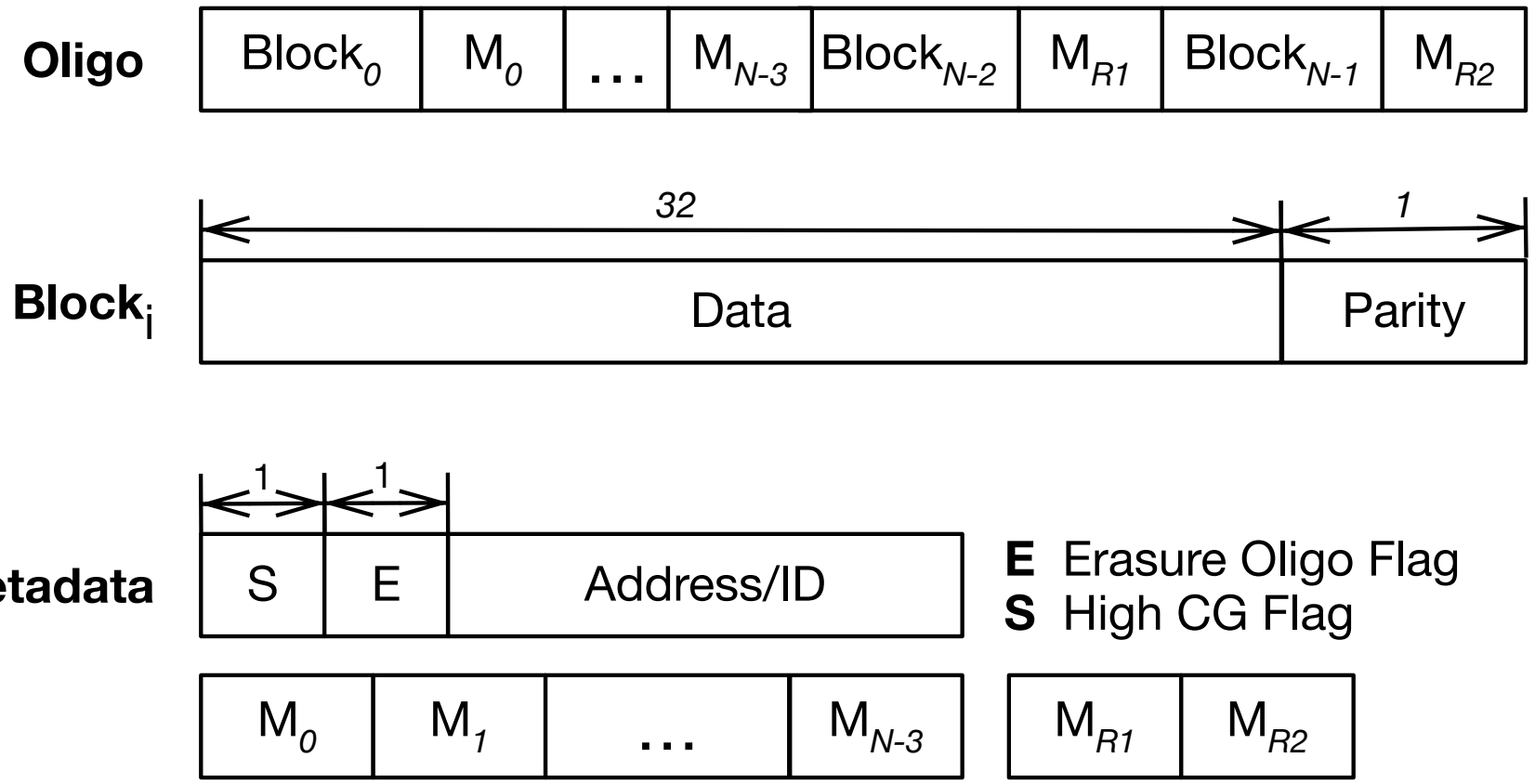
ACOMA Bit Packing (Level 0)

- Same as oligo counting
- Homopolymer restrictions (H4G2):
  - Maximum 4 for A, T, and C
  - Maximum 2 for G
- High CG content: handled at a higher codec level
- It takes exponentially longer time to encode/decode
- Limit up to 17 nts (32 bits data + 1 parity bit)
  - Minimum 10,315,700,031 values (> 2^{33})
  - Data density: 33/17 = **1.94 b/nt**
- Oligo construction:
  - Allows adding up to 17 nts fragments at the end
  - Preserves the homopolymer length restrictions

ACOMA Oligo Layout (Level 1)

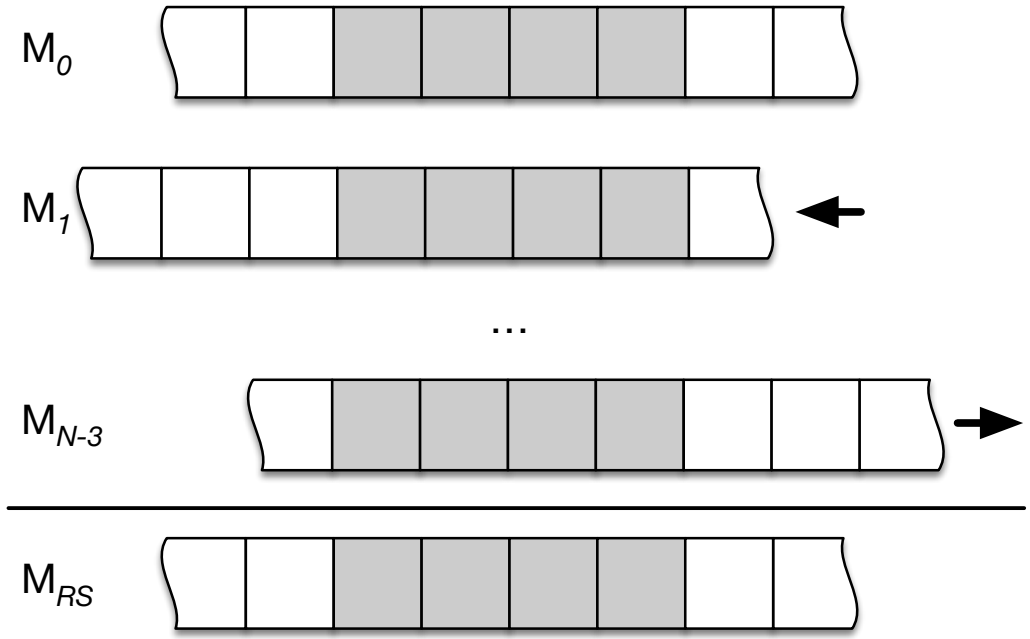
- Data
  - ***N*** 33 bit blocks (32 bit + parity)
- Metadata
  - High CG flag (1 bit)
  - Erasure Oligo flag for Level 2 (1 bit)
  - Address/ID
- Distributed metadata
  - Split into ***N-1*** blocks and place between the data blocks
  - Additional block(s) with Reed-Solomon erasure at the end
  - Used to discover deletions/insertions and align data blocks

ACOMA Oligo Layout (Level 1)



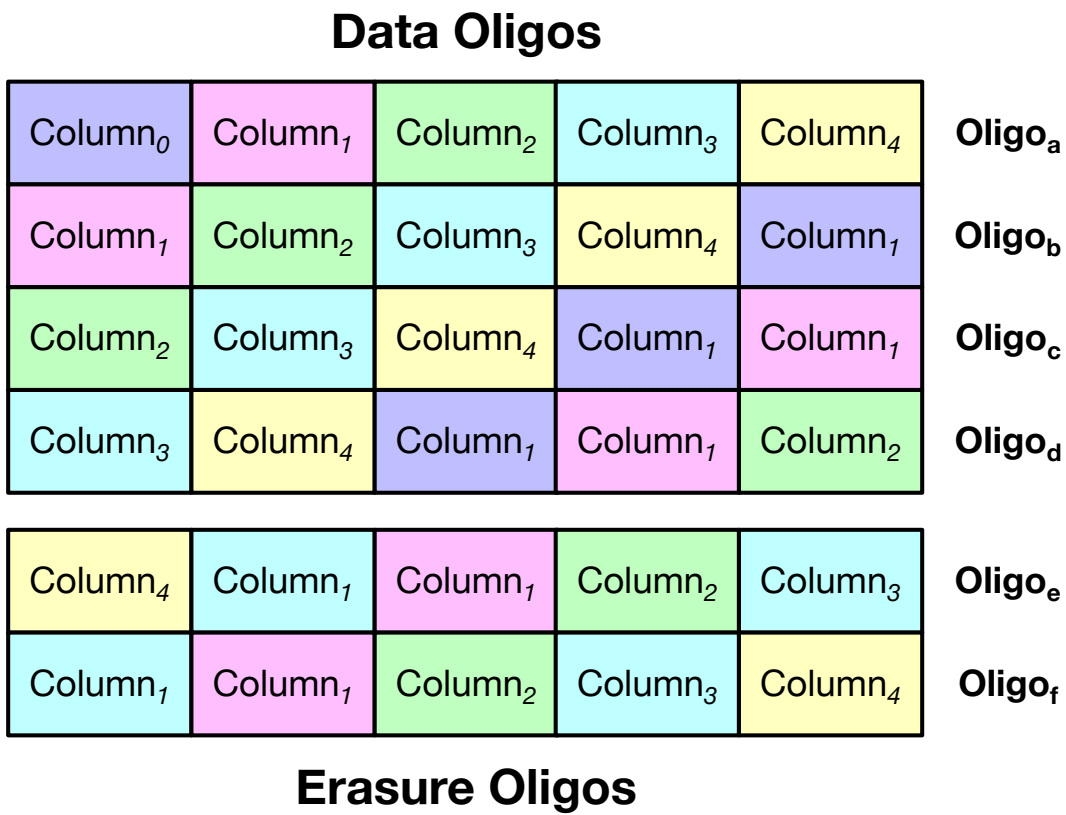
Block Alignment

- Work in progress
- Try to detect insertions and deletions by shifting the metadata blocks
- Shift by 1 left/right and try to match the erasure code
- Needs more analysis on how well it can align blocks *and* correct the metadata



ACOMA Erasure Coding (Level 2)

- 2D erasure encoding
- Group *M* oligos together
- Encode erasure codes for data blocks from different oligos
- Columns consist of blocks from different positions (to correct for spatial bias of errors)
- Reed-Solomon erasure coding
- Parity bit in data blocks used to detect errors



ACOMA Examples

ACOMA Parameters for 107 nt oligos

- 5 data blocks, 17 nts each = 85 nts: **1.94 b/nt**
- 3*4 nts metadata blocks + 2*5 nts RS blocks = 22 nts
- Metadata
  - 4 nts -> 186 values
  - 186^3 = 6,434,856 values
  - 2 bits for High-CG and Erasure-Oligo flags
  - 1608714 addresses/IDs left (30.7 MB)
- Level 1: **1.50 b/nt**
- Erasure Coding
  - 2 (1) Erasure Oligos for every 4 data oligos
  - 4*5*32 bits = 640 data bits per group for 606 (505) nts
- Level 2: **0.996 (1.196) b/nt**

ACOMA Parameters for 110 nt oligos

- 5 data blocks, 17 nts each = 85 nts: **1.94 b/nt**
- 3*5 nts metadata blocks + 2*5 nts RS block = 25 nts
- Metadata
  - 5 nts -> 733 values
  - 733^3 = 393,832,837 values
  - 2 bits for High-CG and Erasure-Oligo flags
  - 98,458,209 addresses/IDs left (1.8 GB)
- Level 1: **1.45 b/nt**
- Erasure Coding
  - 2 (1) Erasure Oligos for every 4 data oligos
  - 4*5*32 bits = 640 data bits per group for 630 (525) nts
  - Level 2: **0.969 (1.163) b/nt**

ACOMA Parameters for 204 nt oligos

- 10 data blocks, 17 nts each = 170 nts: **1.94 b/nt**
- 8*3 nts metadata blocks + 2*5 nts RS blocks = 34 nts
- Metadata
  - 3 nts -> 47 values
  - 47^8 = 23,811,286,661,761 values
  - 2 bits for High-CG and Erasure-Oligo flags
  - 5,952,821,665,440 addresses/IDs left (216 TB)
- Level 1: **1.57 b/nt**
- Erasure Coding
  - 2 (1) Erasure Oligos for every 4 data oligos
  - 4*10*32 bits = 1280 data bits per group for 1182 (985) nts
  - Level 2: **1.045 (1.254) b/nt**

Conclusions

- Adaptive data packing
  - Can use any oligo acceptance criteria, as long is it has reasonable locality
  - Demonstrated good data density with homopolymer restrictions
- Works with different oligo lengths
- Detects deletions and insertions and can align data and metadata blocks
- 2D erasure coding that corrects for spatial error bias and allows multiple erasure oligos

Extra

Implementation: Fast Bit Packing/Unpacking

- Oligo counting is not fast (and exponentially slower)
  - It takes 85 µs on average to encode 13 bit value
  - It takes 2 minutes on average to encode 33 bit value

- Solution: lookup tables
  - For each 4 nts prefix (256 values) generate a table that has the encoding for the first 20 bits of the value (1,048,576 32-bit values, 4 MB)
  - Total space used 1 GB
  - Algorithm:
    1. Pick table based on the previous 4 nts
    2. Lookup in the table the starting oligo using the first 20 bits
    3. Count for the last 13 bits
  - It takes about 1 hour to generate tables, save to disk

Rosetta Stone

- Very long-term storage needs a way to bootstrap
- Oligo(s) that define the ACOMA parameters:
  - Number data blocks per oligo
  - Length of data block (nt)
  - Length of metadata blocks (nt)
  - Number data oligos per erasure group
  - Number of erasure oligos per erasure group
  - **Oligo admission/rejection criteria for bit packing!**
    - Function that receives an oligo and returns true/false
    - Wasm or Knuth's (M)MIX?
  - Encoded with known ACOMA parameters
  - Would be great if it all fits into one oligo

Notes

- Extra data in data block (can we use it for something?)
  - Actual data density is 1.96 b/nt, not 1.94 b/nt ($\log_2(10315700031) = 33.26$)
  - Depending on the 4 nts before the data block, there are some extra values that are lost per data block
  - There is at least an extra bit available for each 4 data blocks
  - Although the minimum number of values in 17 nts is 10,315,700,031 the average number is 13,388,713,708. Can we opportunistically use the extra values, if available?
- Minimum metadata block length
  - 3 nts probably the shortest reasonable length
  - For longer oligos (> 200 nt), instead of making the metadata blocks too small, it may make more sense to add more RS blocks
  - Example: For the 197 nt oligo example, if we have 7 metadata blocks and 2 RS blocks, we'll be able to address 4.6 TB of data.

Implementation: High CG bit

- Problem
  - H4G2 encoding is asymmetric, we can't just use the complementary if high CG

- Solution
  - Encode twice and use the one that has low CG
  - Is it possible that both are high CG?