

# Introduction to DNA data storage

Xavier Pic

January 22nd, 2025

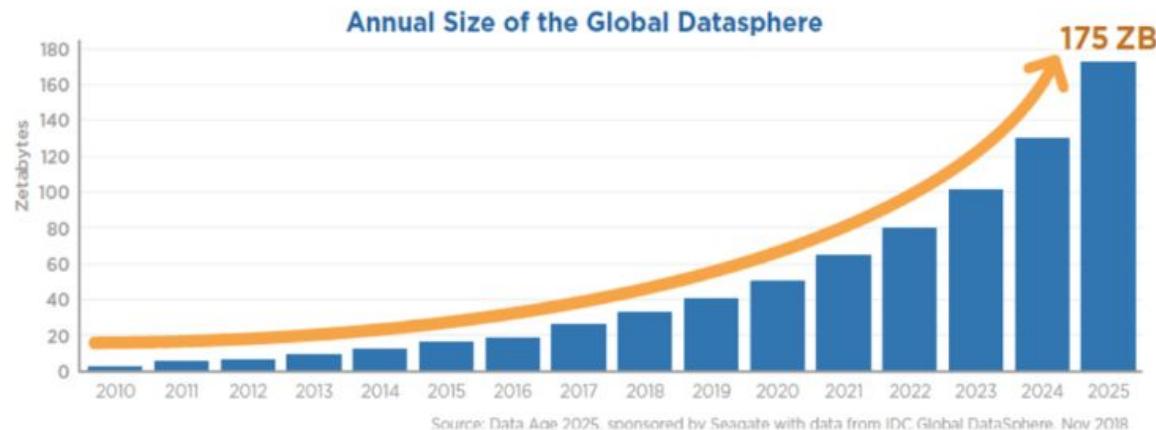
# Contents

- Motivations and principle
- Examples of DNA coders
  - Channel Coders (SFC4 and C3)
  - JPEG-based Image source coders (JPEG DNA SFC4 and JPEG2000 DNA)
  - Direct transcoders adapted to DNA (JPEG DNA VM, CMOSS)

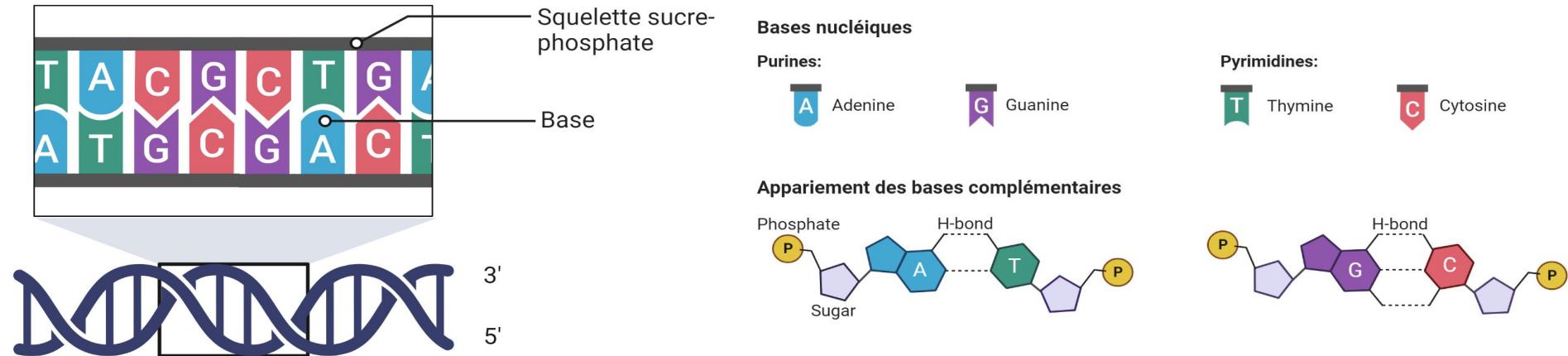
# Motivations and principle

# Conventional Storage Infrastructures

- Data storage demand is **ever expanding**
- Conventional Storage **cannot** be produced in **sufficient quantity**
- High **energy consumption**



# The DNA molecule



# Two key biochemical processes

## Synthesis:

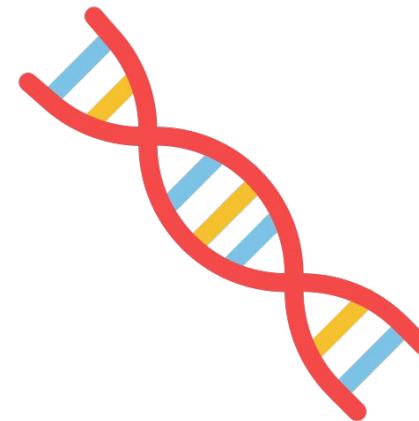
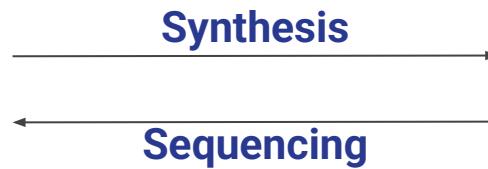
- **Chemical fabrication** of a DNA molecule
- Composed of nucleotides
- Takes as input **any quaternary sequence** composed of As, Ts, Cs and Gs to synthesize in a molecule

## Sequencing:

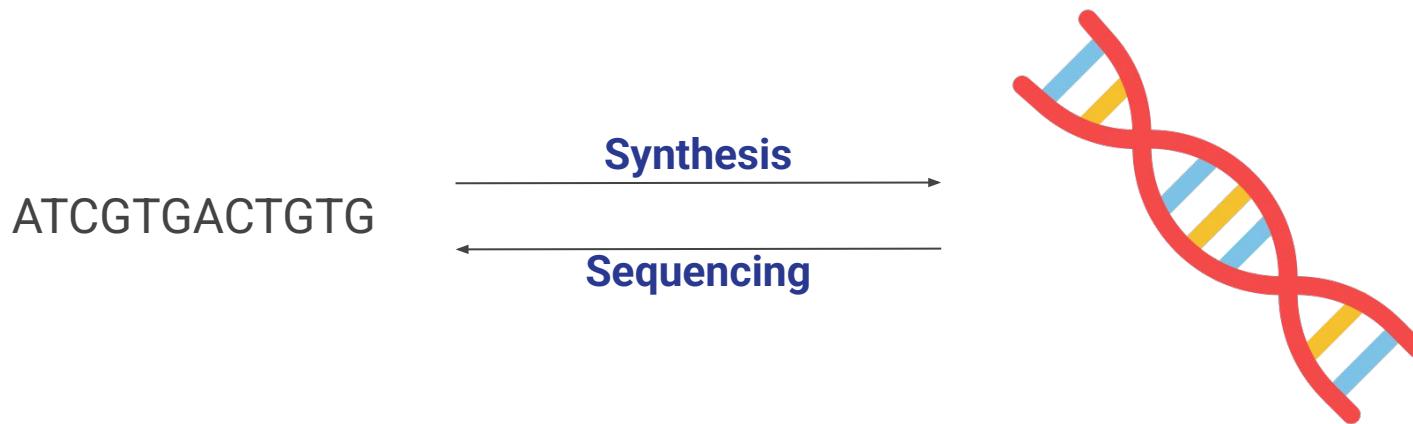
- **Chemical analysis** of a DNA molecule
- **Extracts** the quaternary **sequence** of As, Ts, Cs and Gs composing the molecule
- Takes as input any DNA molecule
- Outputs the associated quaternary representation

# Two key biochemical processes

ATCGTGACTGTG

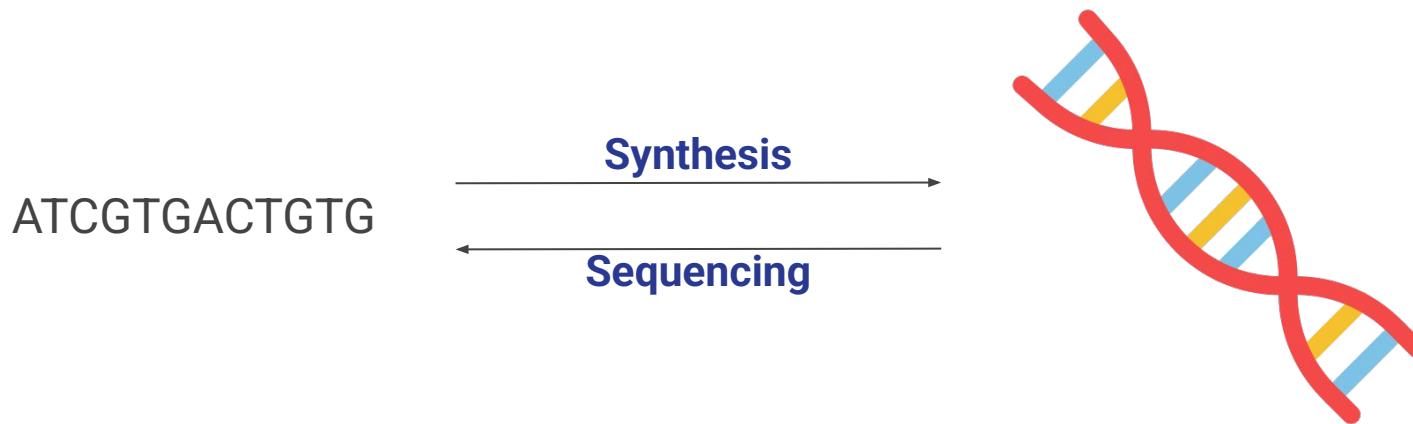


# Through the biologist's lens

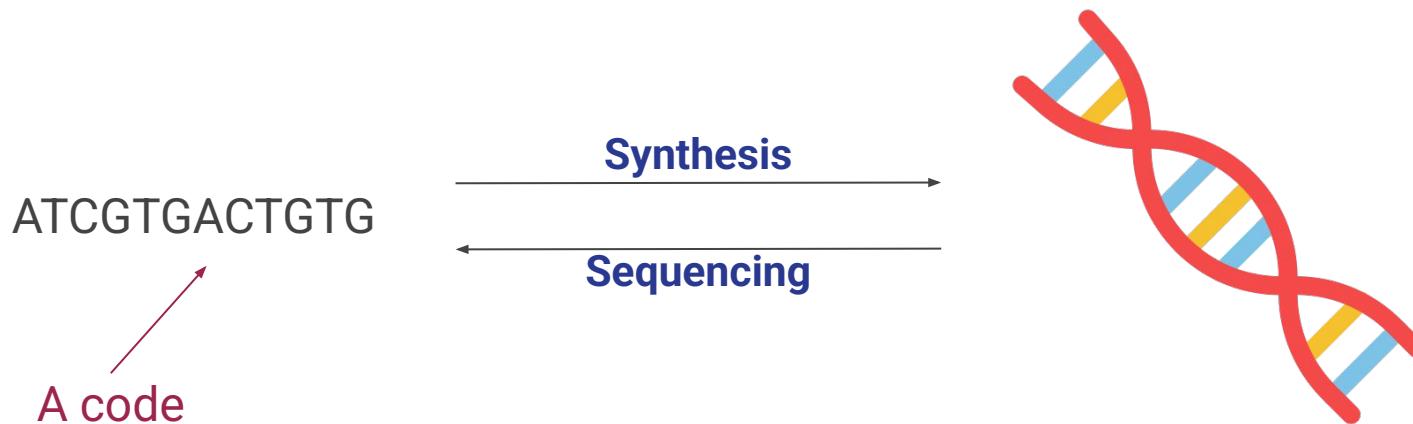


Genome analysis, genetic modification, etc...

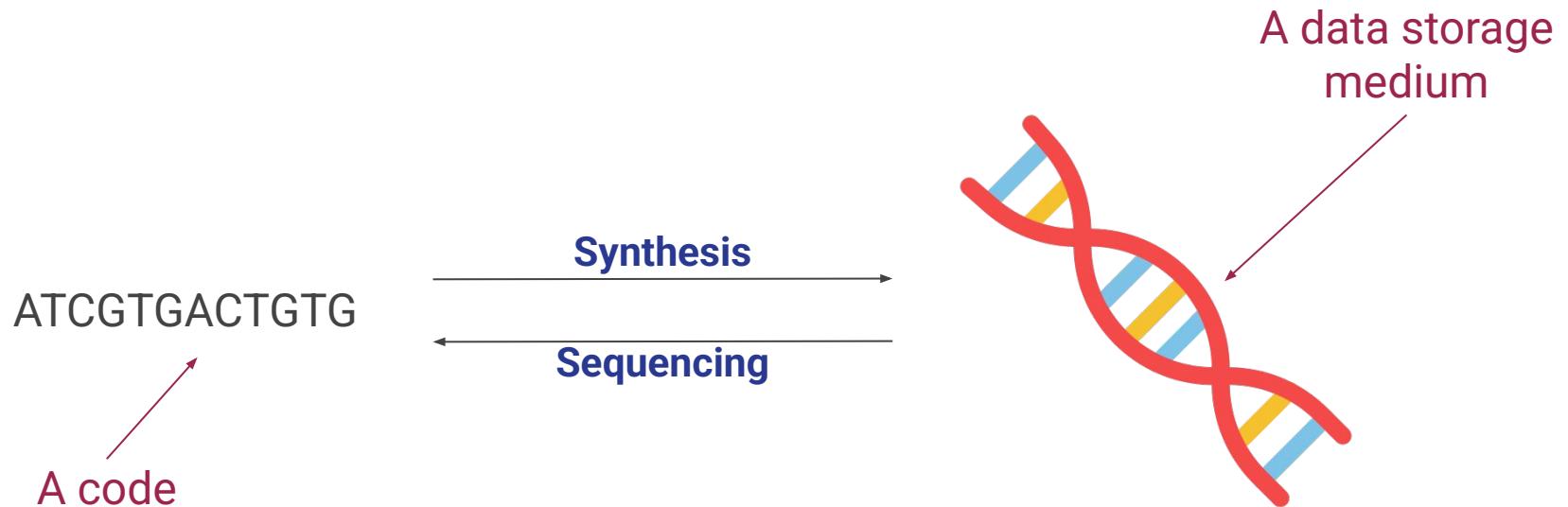
# Through the computer scientist's lens



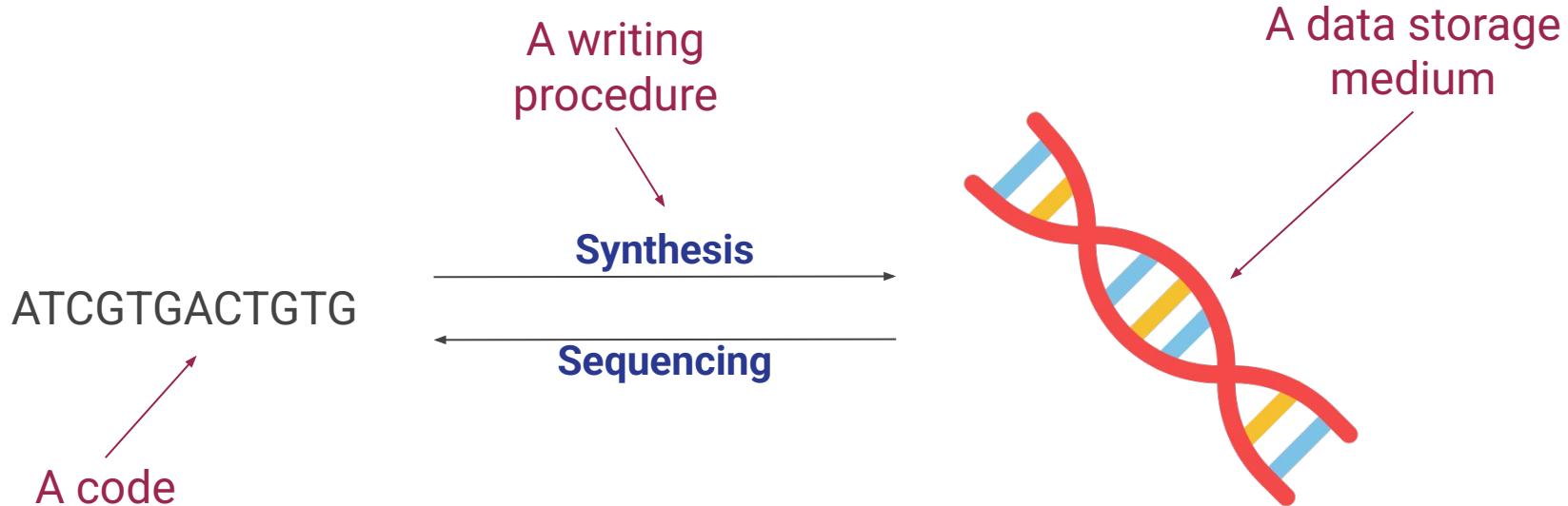
# Through the computer scientist's lens



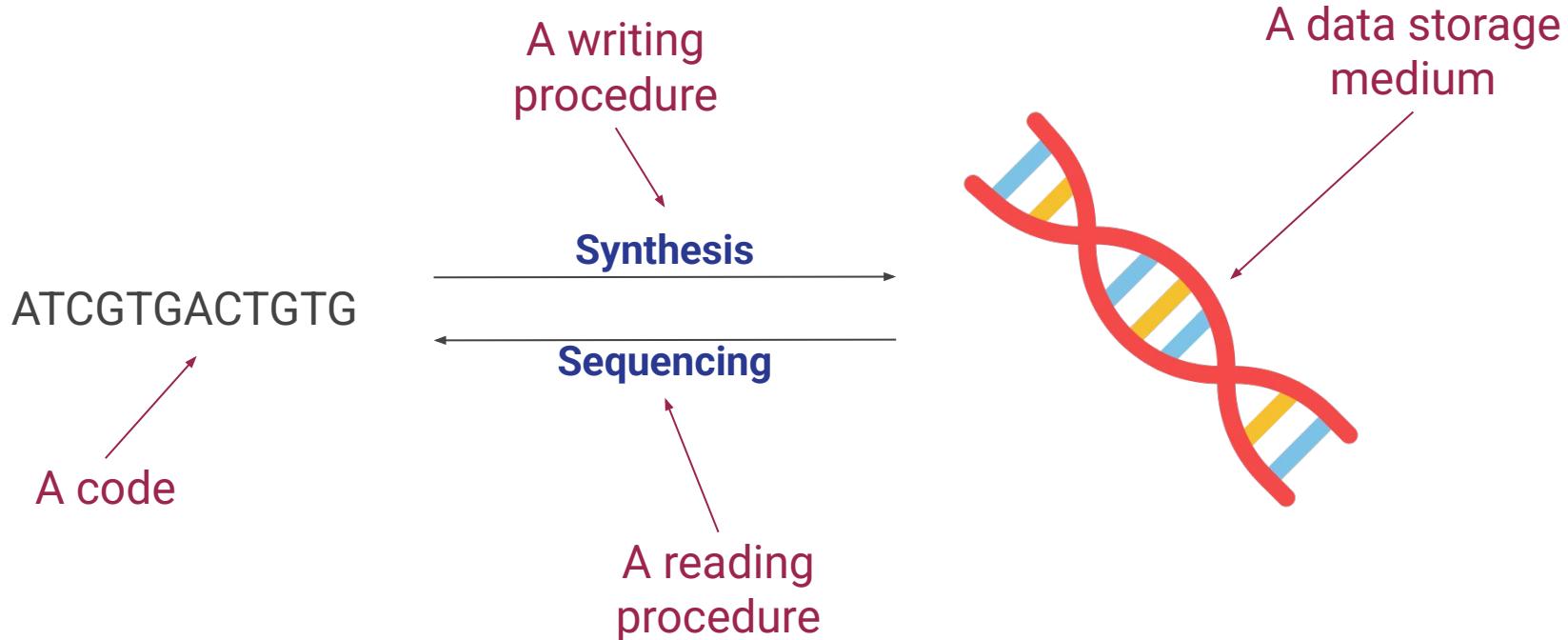
# Through the computer scientist's lens



# Through the computer scientist's lens

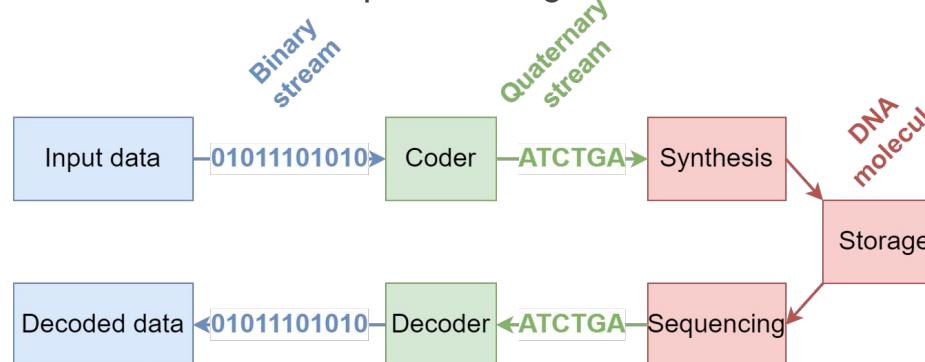


# Through the computer scientist's lens



# DNA Data storage - General Principle

- Writing data:
  - Encode a file into a set of quaternary sequences (oligos)
  - Synthesize the DNA molecules represented by these sequences
  - Store the molecules
- Reading data:
  - Retrieve the quaternary sequences from the stored DNA molecules (sequencing)
  - Decode the file from the set of sequenced oligos



**Fig:** General workflow of DNA data storage

# DNA Data storage - Biochemical operations

- Synthesis : Create a set of DNA molecules
- PCR : Copy molecules of DNA
- Sequencing : Read the structure of the DNA molecules

Operation	Cost	Speed	Errors
<b>Synthesis</b>	Very High	Very Slow	Few
<b>PCR</b>	Low	Fast	Low
<b>Sequencing</b>	High	Slow	Many

# DNA Coding - Principle

## Binary File (.png)

00000000: 00001001 01010000 01001110 01000111 00001101 00001010 ..PNG..  
00000006: 000011010 00001010 00000000 00000000 00000000 00001101 ..  
0000000c: 010001001 01001000 00001001 01010010 00000000 00000000 ..IHDR..  
00000012: 00000011 00000000 00000000 00000000 00000010 00000000 ..  
00000018: 00001000 00000000 00000010 00000000 00000000 00000000 100111010 ..  
0000001e: 100011000 100111000 01011101 01001101 00000000 00000000 ..m..  
00000024: 000000100 01000111 01000001 01001101 01000001 00000000 ..gAMA..  
0000002a: 000000000 10100001 00001111 00000000 11111000 01000001 ..a..  
00000030: 000000101 00000000 00000000 00000000 00000001 01100011 ..s..  
00000036: 010001000 010000111 01000000 00000000 10101110 11001110 ..RGB..  
0000003c: 000011000 111010001 00000000 00000000 00000000 00000000 00001000 ..  
00000042: 011101000 010000101 01011000 01100100 01100001 01010001 tExTs0..  
00000048: 011101001 01100010 01000001 01100101 00000000 00000000 00000000 ..urc..K..  
0000004e: 011001111 01100000 01100001 01100101 00100000 01010000 odak P..  
00000054: 010000000 00000000 00000000 00000000 00000001 00100010 D...C9992..  
00000055: 010000100 100111001 00000000 01000000 00000000 00000000 00000000 ..D..  
00000060: 000000000 000000000 01000001 00000000 01000001 01010000 ..IDAT..  
00000066: 011100000 110011010 110011000 110011001 01010000 00000000 ..x..W..  
0000006c: 010011111 110011001 100110001 00000000 01100000 11000000 ..v..  
00000072: 000000000 101000001 010000001 011000001 10010000 01100000 ..a..v..  
00000078: 010000000 000000000 000000000 000000000 000000000 000000000 F3#1..  
0000007e: 010000000 011000000 000000000 000000000 000000000 000000000 Gv7s.9..  
00000084: 100000000 110000000 010000000 000000000 000000000 000000000 ..  
00000088: 011000000 110000000 000000000 000000000 000000000 010000000 s.9.bU..  
00000090: 100000001 000000001 010000000 000000000 000000000 000000000 ..E..9..  
00000096: 001000000 010000000 000000000 000000000 000000000 000000000 ..6..  
0000009c: 010000000 110000000 000000000 000000000 000000000 000000000 Z...vvv..  
000000a2: 000000000 000000000 000000000 000000000 000000000 11110000 ../.0..  
000000a8: 110000001 000000000 000000000 000000000 000000000 11110000 ..1..  
000000ae: 000000000 110000001 000000000 000000000 000000000 10000000 ..  
000000b4: 011110001 010000000 011111111 000000000 000000000 000000000 }^..=..  
000000ba: 000000000 110000000 000000000 000000000 000000000 000000000 ..vw\$kg..  
000000c0: 011100000 110000000 000000000 000000000 000000000 100000000 w...8..  
000000c6: 100000000 000000000 000000000 000000000 000000000 111100000 ..  
000000cc: 000000000 100000000 000000000 000000000 000000000 110000000 ..  
000000d2: 110000000 000000000 000000000 000000000 000000000 100000000 ..  
000000d8: 111111111 000000000 000000000 000000000 000000000 111111111 ..\br/>000000de: 111111111 111111111 000000000 000000000 000000000 111111111 ..  
000000e4: 111111111 000000000 111111111 000000000 000000000 111111111 ..  
000000ea: 011111111 000000000 000000000 111111111 000000000 100000000 ..?..  
000000f0: 111111001 111110000 000000000 111110000 000000000 100000000 ..%..  
000000f6: 100000001 000000001 000000001 000000001 000000001 111111111 ..%.  
000000fc: 010000001 000000001 000000001 000000001 000000001 111111110 IK..1..  
00000102: 010000001 000000001 000000001 000000001 000000001 100000000 S....  
00000108: 011111100 000000000 000000000 000000000 000000000 110000000 ..?..

## ENCODING

## DECODING

## DNA File (.fasta)

# DNA Coding - Constraints

The following operations can increase the errors in biochemical processes (synthesis, PCR, sequencing):

- Homopolymers (repetition of the same nucleotide)
- Motifs (patterns)
- Unbalanced GC content
- Large sequences (>300 nts)
- Undesired sequences



ADAPT AND CONSTRAIN THE CODING SYSTEM

# DNA Coding - Why do we need to compress the data?

Errors can occur in the biochemical processes (synthesis, sequencing, PCR):

- High sequencing cost
- Very high synthesis cost
- Low synthesis and sequencing speed (writing and reading cost)



REDUCE THE SIZE OF THE ENCODED DNA FILES

# Examples of DNA coders

# Summary of the presentation - DNA coding methods

- DNA Adapted Channel coders:
  - SFC4
  - C3
  - CM OSS
- Image coders adapted to DNA:
  - JPEG DNA VM
  - JPEG DNA SFC4
  - JPEG 2000 DNA
  - HiDNA

# Examples of DNA Channel Coders

SFC4

# DNA Channel Coders - Entropy coder

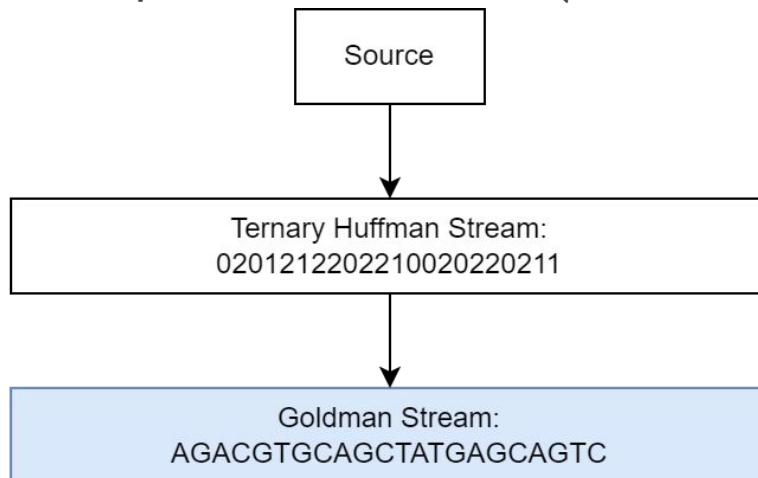
- **Variable length** coder
- Adapted to **i.i.d. sources**
- Length of the codeword depends on the **probability of appearance** of the associated symbol
- Better performance for compression

Symbol	Probability	Code
a	0.40	0
b	0.05	1010
c	0.18	110
d	0.07	1011
e	0.20	111
f	0.10	100

**Fig:** Example of a binary Huffman code

# DNA Channel Coders - The Goldman Coder

- Ternary Huffman Entropy Coder
- No repeated nucleotides (no homopolymers)



Previous nucleotide	0	1	2
A	T	C	G
T	A	C	G
C	A	T	G
G	A	T	C

**Fig:** Ternary to DNA translation table

**Fig:** The data is first encoded into a ternary code

N. Goldman, P. Bertone, and S. Chen, "Towards practical, high-capacity, low-maintenance information storage in synthesized dna," *Nature*, 2013.

# Performance metrics - DNA entropy coders

Expected length:

$$\mathcal{L}(C) = \sum_{x \in \Omega} p(X = x)l(C_x)$$

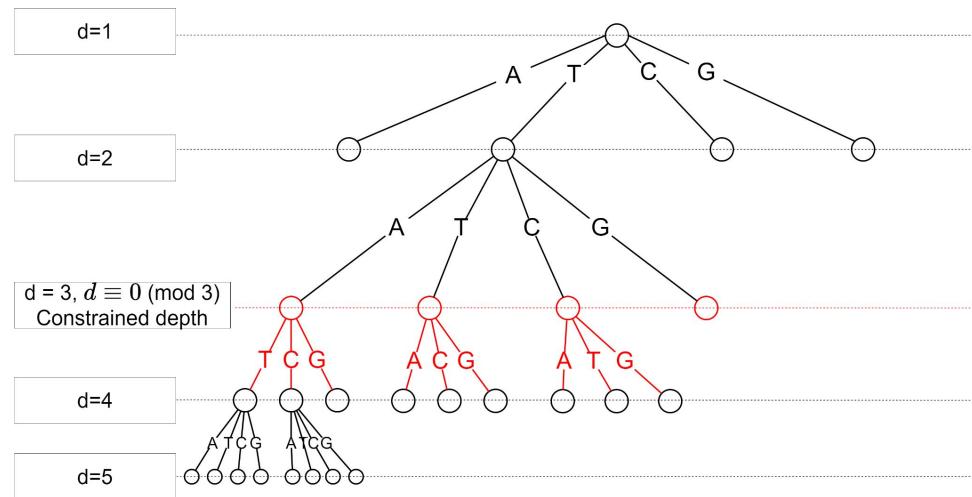
- $\Omega$  - The set of symbols in the source
- $C_x$  - The codeword associated to the symbol
- $l(C_x)$  - The length of a codeword

The **average size of a code** output by the entropy coder for a source

In the case of DNA coding, it is expressed in **nucleotides per symbol**

# SFC4 - Characterization of the source and principle

- A source  $S$  composed of elements of an alphabet  $A$  has to be encoded
- The frequency of appearance of each element of  $A$  in  $S$  is computed
- A tree  $T$  is initialized as a single node (the root) where all the symbols are allocated
- The Shannon Fano tree is built by subdividing the leaves of the tree



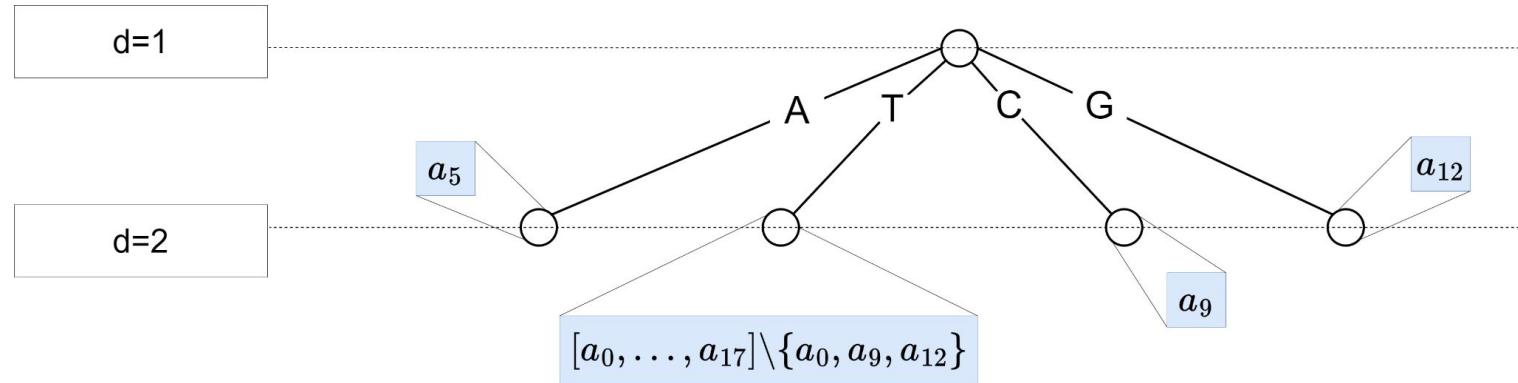
**Fig.:** Example of an SFC4 coding tree, constrained at depths multiples of 3

# SFC4 - Coding tree



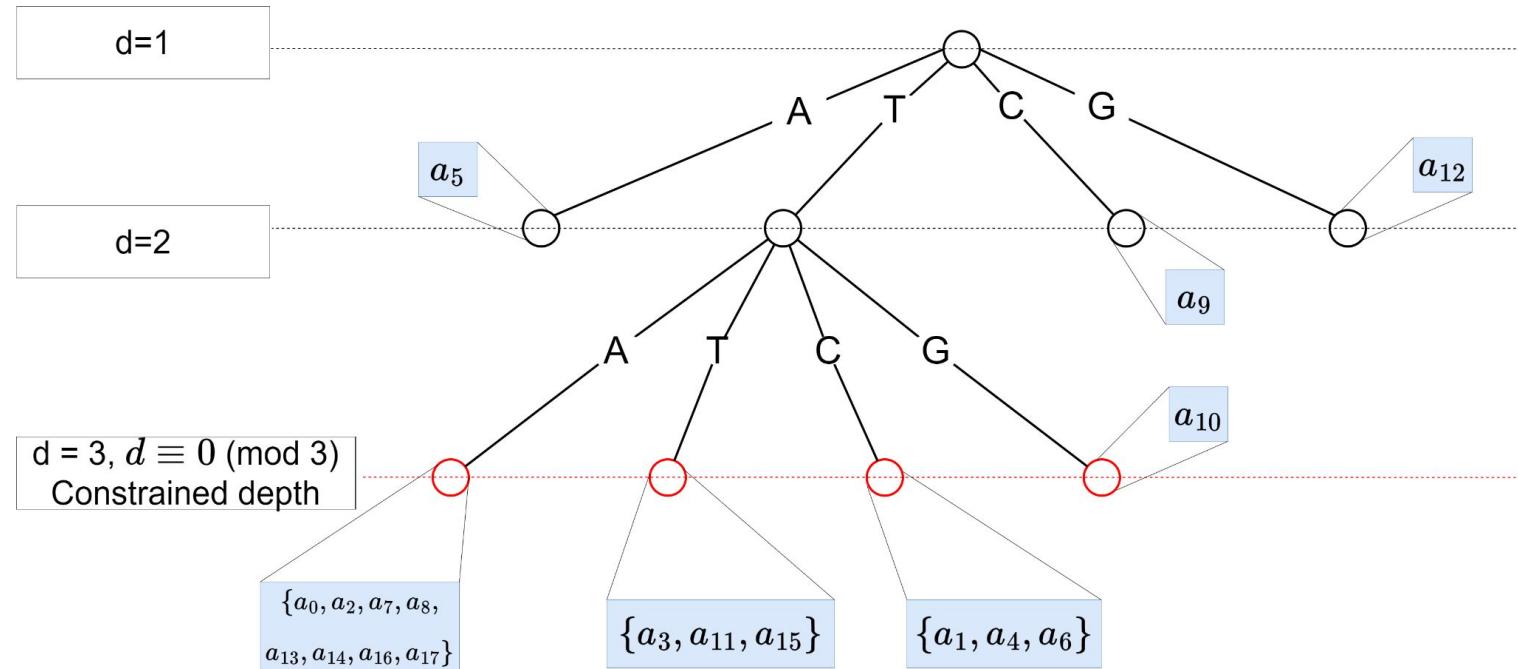
**Fig.:** Example of an SFC4 coding tree, constrained at depths multiples of 3

# SFC4 - Coding tree



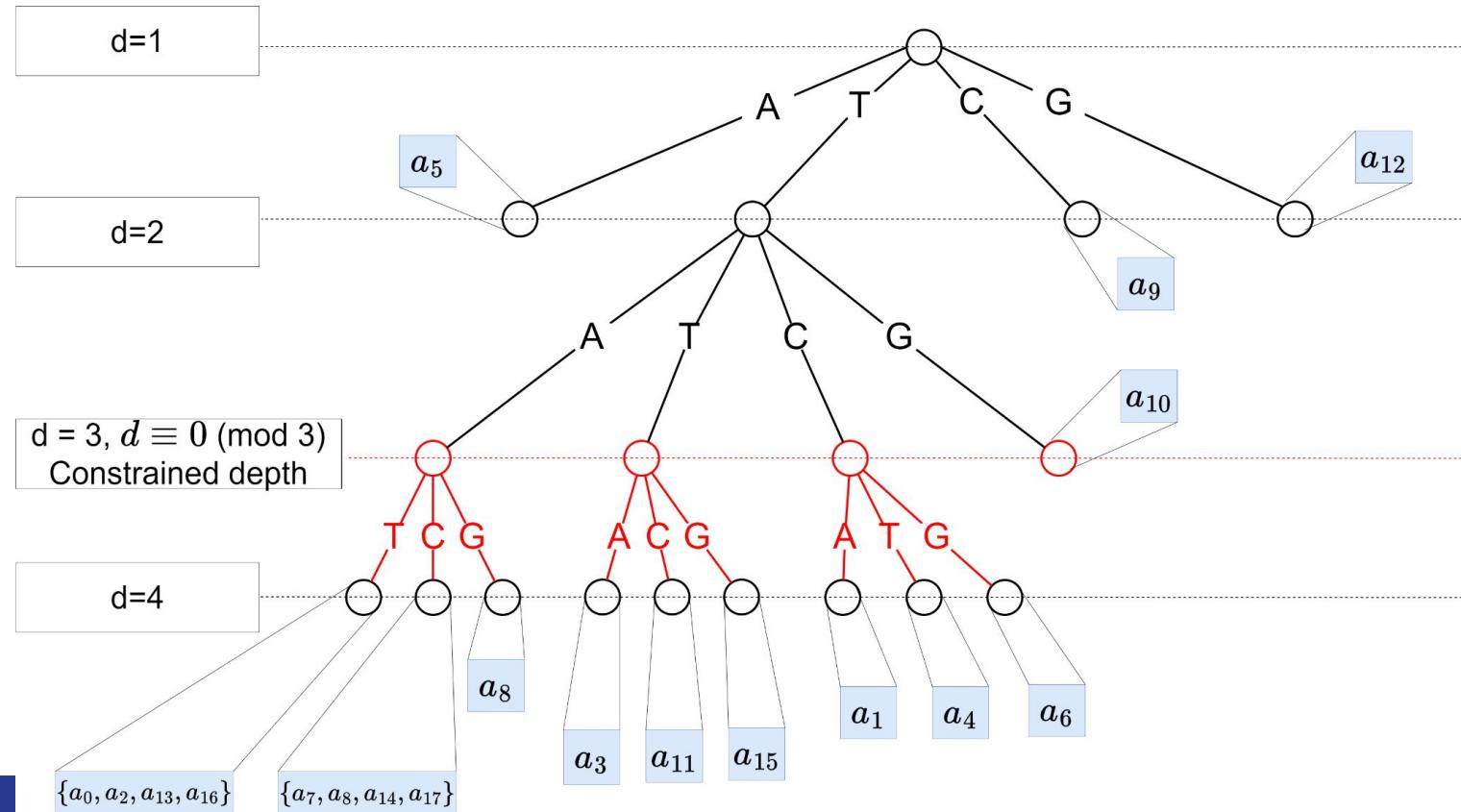
**Fig.:** Example of an SFC4 coding tree, constrained at depths multiples of 3

# SFC4 - Coding tree

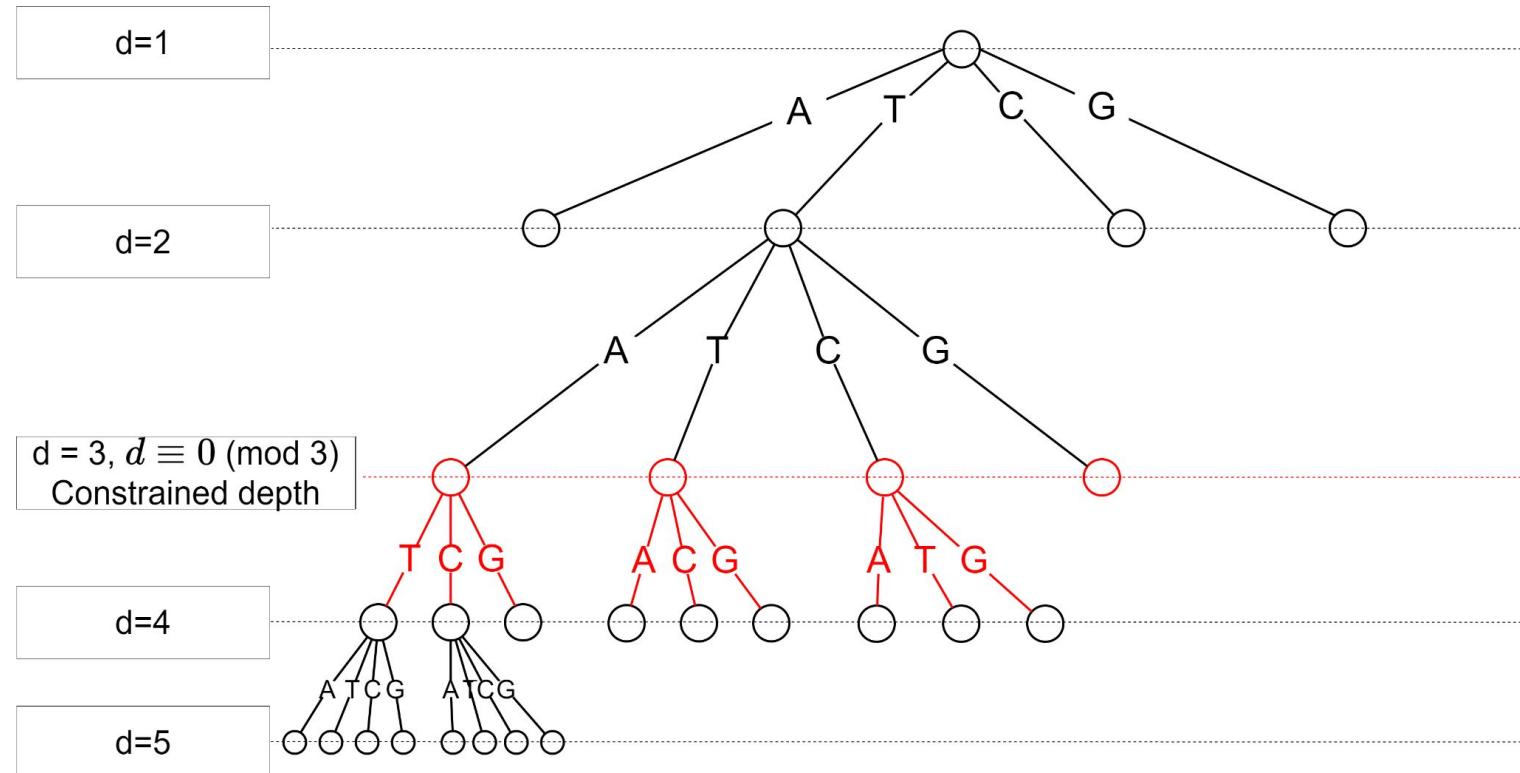


**Fig.:** Example of an SFC4 coding tree, constrained at depths multiples of 3

# SFC4 - Coding tree



# SFC4 - Coding tree



**Fig.:** Example of an SFC4 coding tree, constrained at depths multiples of 3

# SFC4 - Results on I.I.D. Gaussian Sources

Expected length:

- Average results on a series of **100 i.i.d. gaussian sources**
- Each source contained **10000 samples**
- Quantized to the **nearest integer**

$H_4(X)$	$L(C_{SFC4})$	$H_3(X)$	$L(C_{HG})$
3.48	<b>3.81</b>	4.39	4.45

**Fig:** Ternary to DNA translation table

# Examples of DNA Channel Coders

C3DNA

## C3 - Principle of the MQ coder's arithmetic coder

- Source: [1,0,1,1 ]
- Initialize an interval to [0, 1]

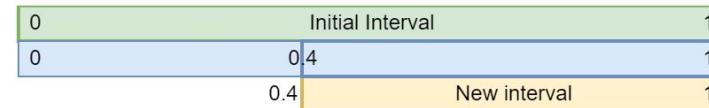
Received bits	1011	
<b>Event</b>	<b>Actions</b>	<b>Intervals</b>
None	Start	$I = [0, 1)$



# C3 - Principle of the MQ coder's arithmetic coder

- Source: [1,0,1,1 ]
- Initialize an interval to [0, 1]
- First received bit: 1
  - Subdivide the interval into two smaller intervals of size relative to the probability of appearance of a zero or a one.
  - Select the subdivision associated to the received bit (1)

Received bits	1011	
Event	Actions	Intervals
None	Start	$I = [0, 1]$
Received 1	Subdivision Selection	$[0, 0.4), [0.4, 1)$ $I = [0.4, 1)$



# C3 - Principle of the MQ coder's arithmetic coder

- Source: [1,0,1,1 ]
- Initialize an interval to [0, 1]
- First received bit: 1
- Second received bit: 0
  - Subdivide the interval into two smaller intervals of size relative to the probability of appearance of a zero or a one.
  - Select the subdivision associated to the received bit (0)

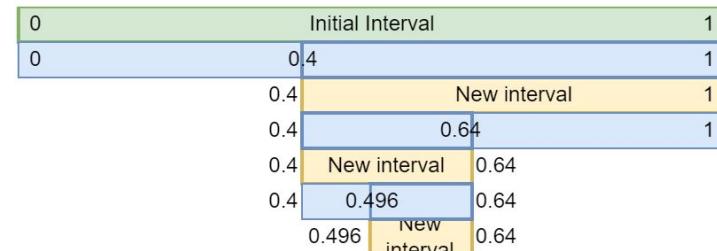
Received bits	1011	
Event	Actions	Intervals
None	Start	I = [0, 1)
Received 1	Subdivision	[0, 0.4), [0.4, 1)
	Selection	I = [0.4, 1)
Received 0	Subdivision	[0.4, 0.6*0.4+0.4=0.64),[0.64, 1)
	Selection	I = [0.4, 0.64)



# C3 - Principle of the MQ coder's arithmetic coder

- Source: [1,0,1,1 ]
- Initialize an interval to [0, 1]
- First received bit: 1
- Second received bit: 0
- Third received bit: 1
  - Subdivide the interval into two smaller intervals of size relative to the probability of appearance of a zero or a one.
  - Select the subdivision associated to the received bit (1)

Received bits		1011
Event	Actions	Intervals
None	Start	I = [0, 1)
	Subdivision	[0, 0.4), [0.4, 1)
Received 1	Selection	I = [0.4, 1)
	Subdivision	[0.4, 0.6*0.4+0.4=0.64),[0.64, 1)
Received 0	Selection	I = [0.4, 0.64)
	Subdivision	[0.4, 0.496), [0.496, 0.64)
Received 1	Selection	I = [0.496, 0.64)



# C3 - Principle of the MQ coder's arithmetic coder

- Source: [1,0,1,1 ]
- Initialize an interval to [0, 1]
- First received bit: 1
- Second received bit: 0
- Third received bit: 1
- Final received bit: 1

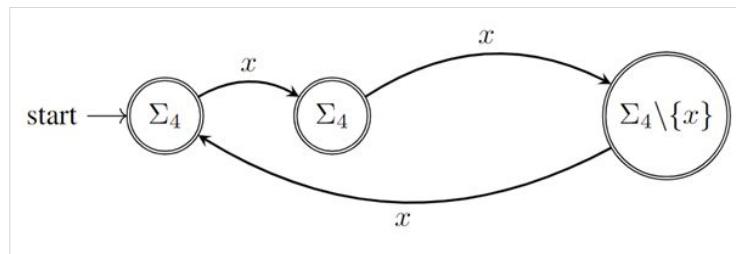
1011		
Received bits		
Event	Actions	Intervals
None	Start	$I = [0, 1)$
Received 1	Subdivision	[0, 0.4), [0.4, 1)
	Selection	$I = [0.4, 1)$
Received 0	Subdivision	[0.4, 0.6*0.4+0.4=0.64), [0.64, 1)
	Selection	$I = [0.4, 0.64)$
Received 1	Subdivision	[0.4, 0.496), [0.496, 0.64)
	Selection	$I = [0.496, 0.64)$
Received 1	Subdivision	[0.496, 0.5536), [0.5536, 0.64)
	Selection	$I = [0.5536, 0.64)$
Output		$x=0.625$
p0=0.4, p1=0.6	x is the element of I with the shortest binary representation	

The diagram illustrates the iterative subdivision of the initial interval [0, 1) into smaller intervals. The process starts with the initial interval [0, 1). As each bit is received, the current interval is subdivided into two new intervals. The 'New interval' is highlighted in yellow. The 'Old interval' is shown in blue. The 'End' point of the final interval is highlighted in red. The final interval is [0.5536, 0.64).

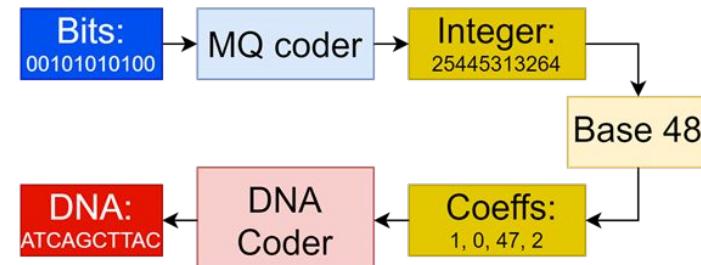
The **final interval** represents the whole input source [1, 0, 1, 1]

# C3 - MQ coder-based arithmetic coder for DNA

- Transcode the registries of the binary MQ-coder
- Constrained fixed length code of length 3 (48 elements)
- Transcode integers into a base 48 representation
- Code the coefficients of this representation



**Fig.** Automata generating the coding dictionary: **homopolymers are avoided**



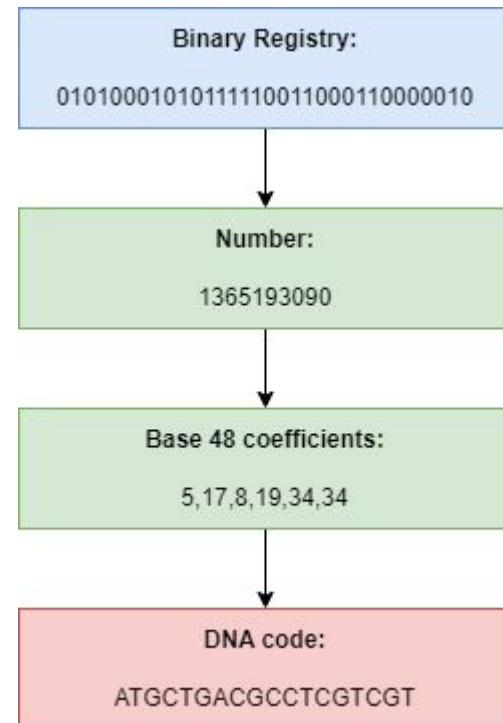
**Fig.** Adaptation of the MQ-coder to DNA

$$C_3 = \{AAT, AAC, AAG, ATA, ATC, ATG, ACA, \dots, GCT, GCG, GGA, GGT, GGC\}$$

# C3 - Encoding a registry

- The registry is first converted into a number
- The number is represented into base 48
- The coefficients in base 48 are encoded into DNA, one by one, with the C3 coder:

$$C_3 = \{AAT, AAC, AAG, ATA, ATC, ATG, ACA, \dots, GCT, GCG, GGA, GGT, GGC\}$$

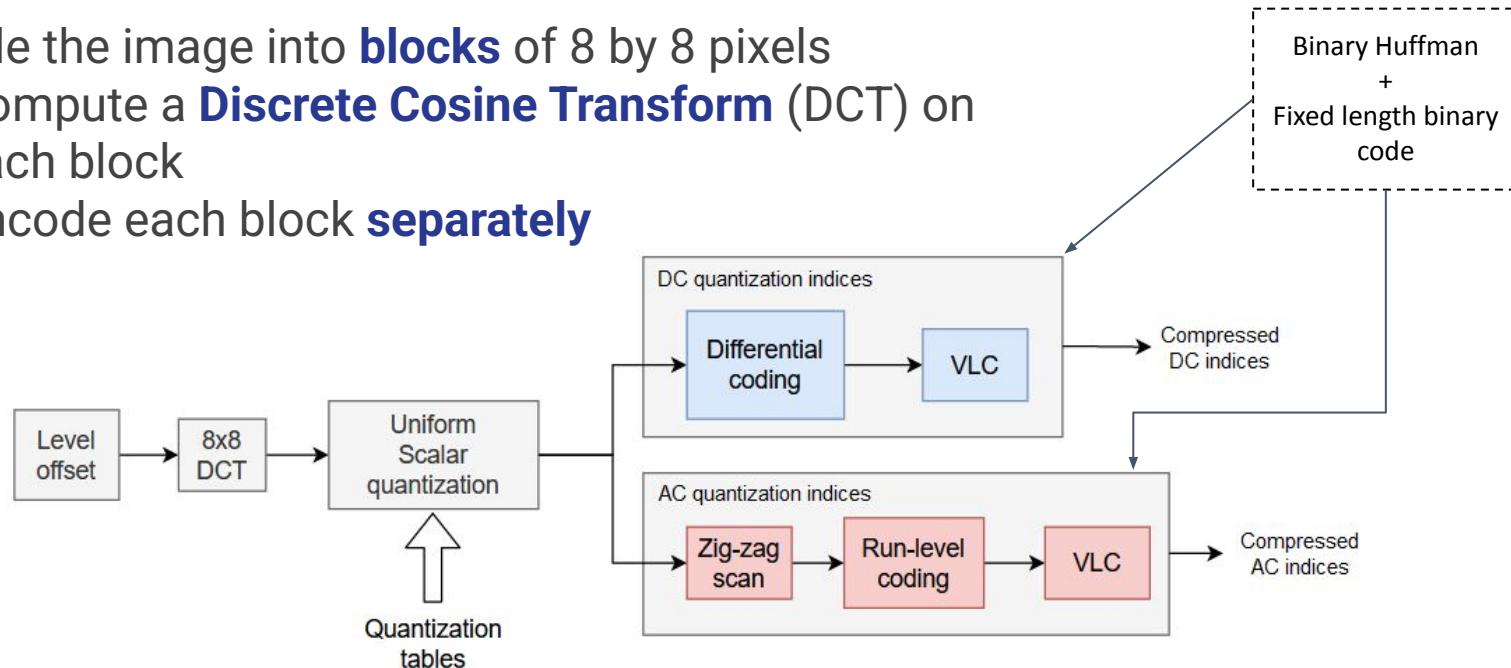


# Examples of DNA Image Coders

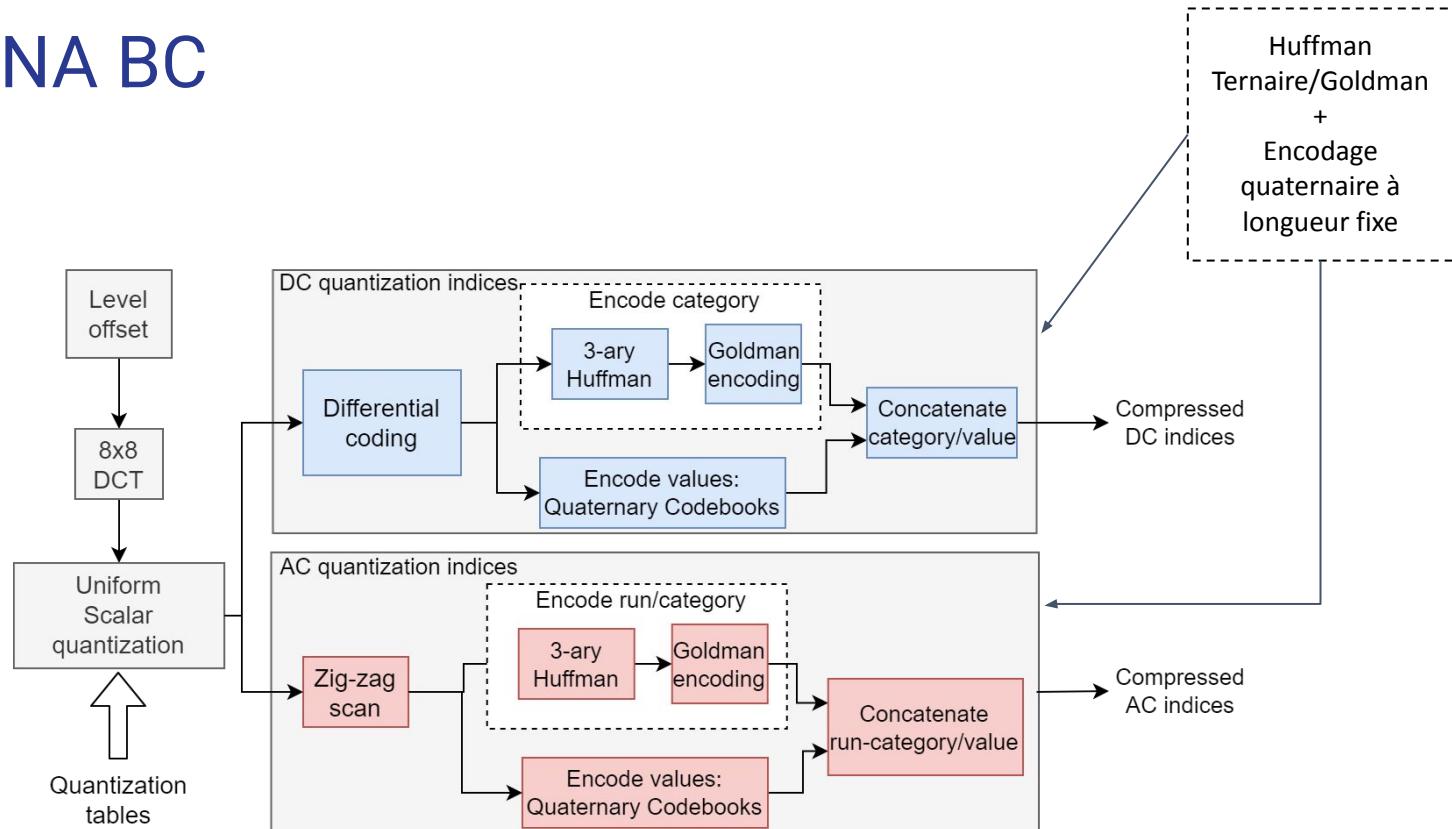
JPEG DNA SFC4 and JPEG2000 DNA

# Image coders - JPEG

- Tile the image into **blocks** of 8 by 8 pixels
- Compute a **Discrete Cosine Transform** (DCT) on each block
- Encode each block **separately**

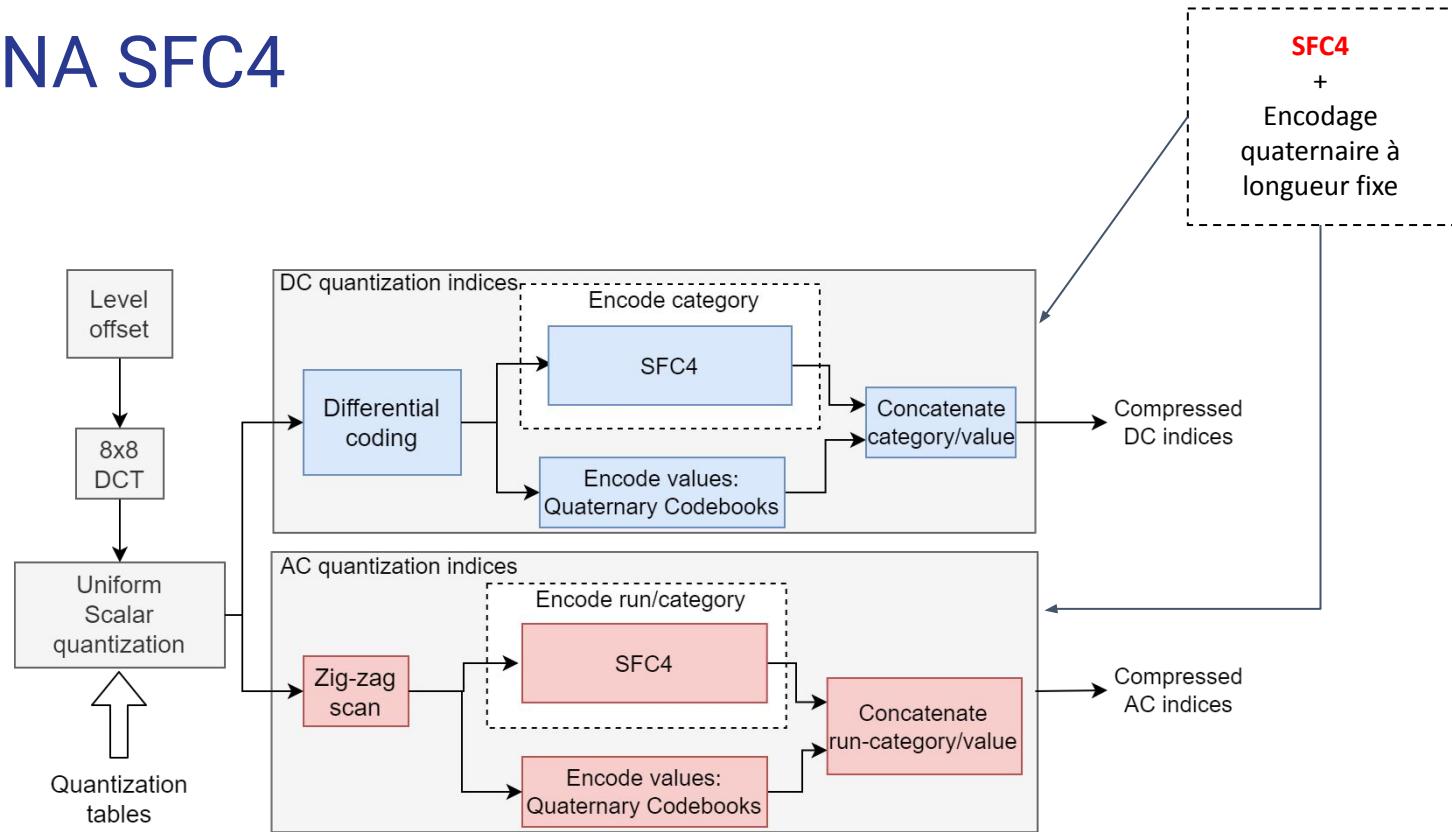


# JPEG DNA BC



1. M. Dimopoulou, E. Gil San Antonio, M. Antonini, "A JPEG-based image coding solution for data storage on DNA", *EUSIPCO*, 2021.
2. X. Pic, E. Gil San Antonio, M. Dimopoulou, M. Antonini, M93103 - JpegDNA Python Library

# JPEG DNA SFC4



# Metrics for DNA coding

# Performance metrics - DNA Channel coders

Compression rate:

$$cr_{btsnt} = \frac{\#bits}{\#nucs}$$

The **number of bits** in the source that can be encoded in a **single nucleotide**

# Performance metrics - DNA image coders

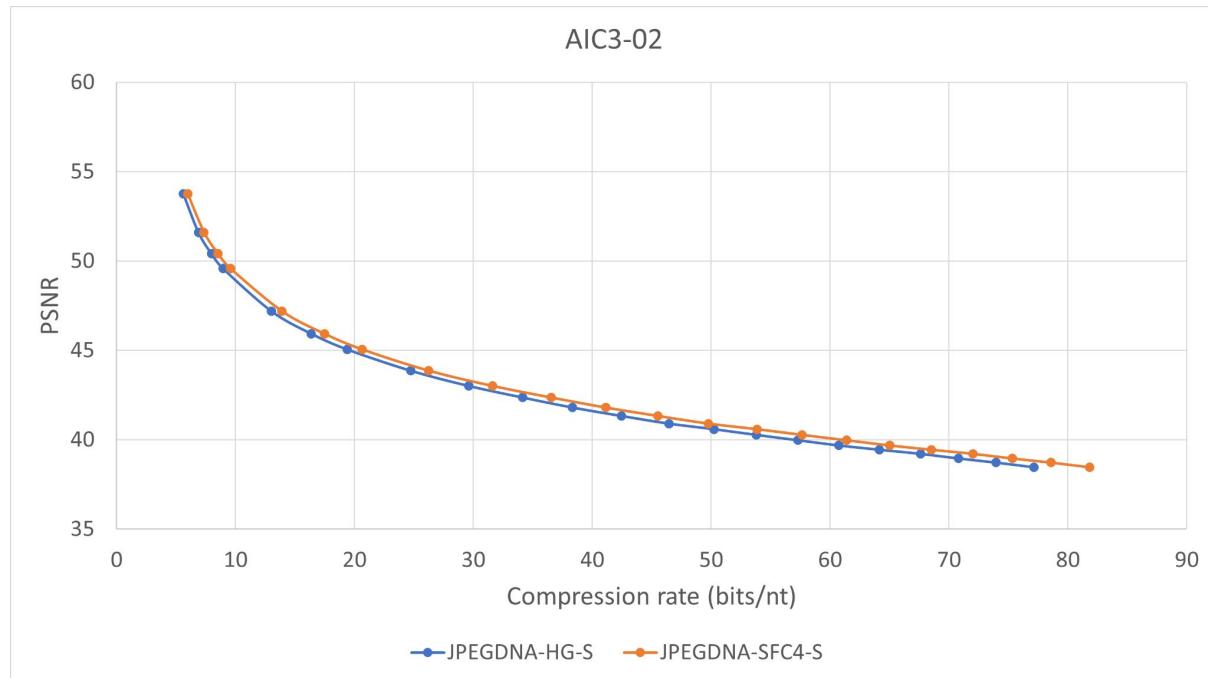
Nucleotide rate:

$$r_{ntpp} = \frac{\#nucs}{H \times W}$$

The **average number of nucleotides** to encode a **pixel**

# JPEG DNA SFC4 - Results

- Novel codec improves the rate by 5% on average
- Tested on different datasets (kodak and JPEG AIC 03)



1. Kodak dataset, weblink: <https://r0k.us/graphics/kodak/>
2. M. Testolina, V. Hosu, M. Jenadeleh, D. Lazzarotto, D. Saupe, T. Ebrahimi, "JPEG AIC-3 Dataset: Towards Defining the High Quality to Nearly Visually Lossless Quality Range", 2023 15th International Conference on Quality of Multimedia Experience (QoMEX), Ghent, Belgium, 2023

# JPEG2000 DNA - Principle

- The **binary MQ coder** is associated to the new **C3 coder**
- The **overheads** are transcoded into DNA using a **fixed length** DNA adapted coder
- The decoder consists in reverting all previous operations
- **Closed loop modification** of JPEG2000

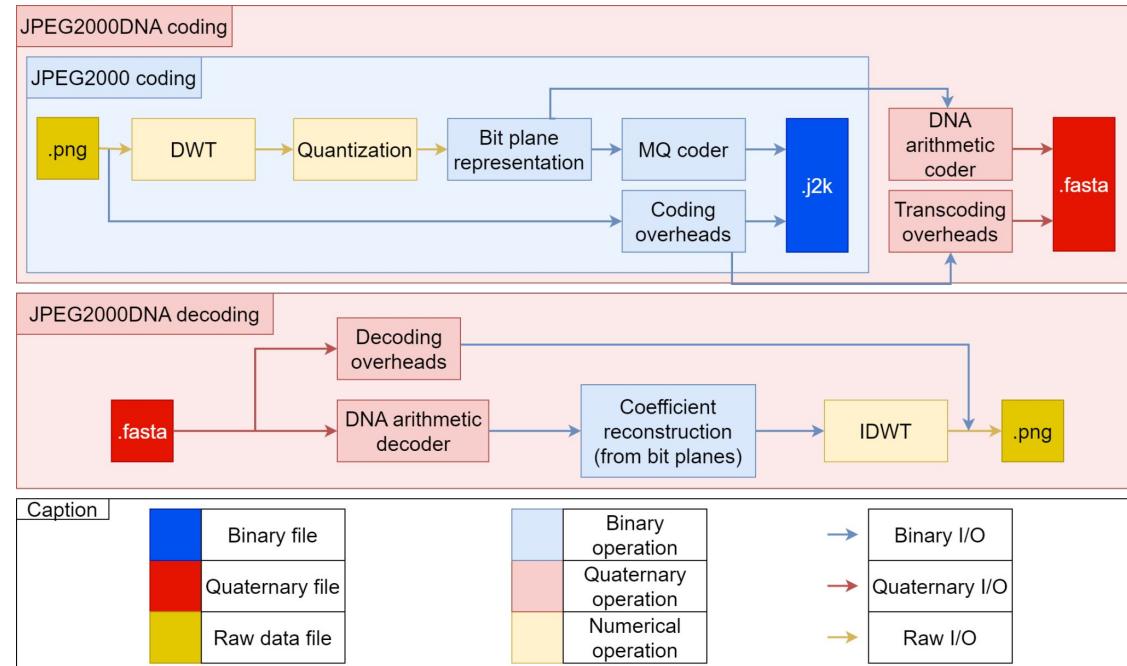
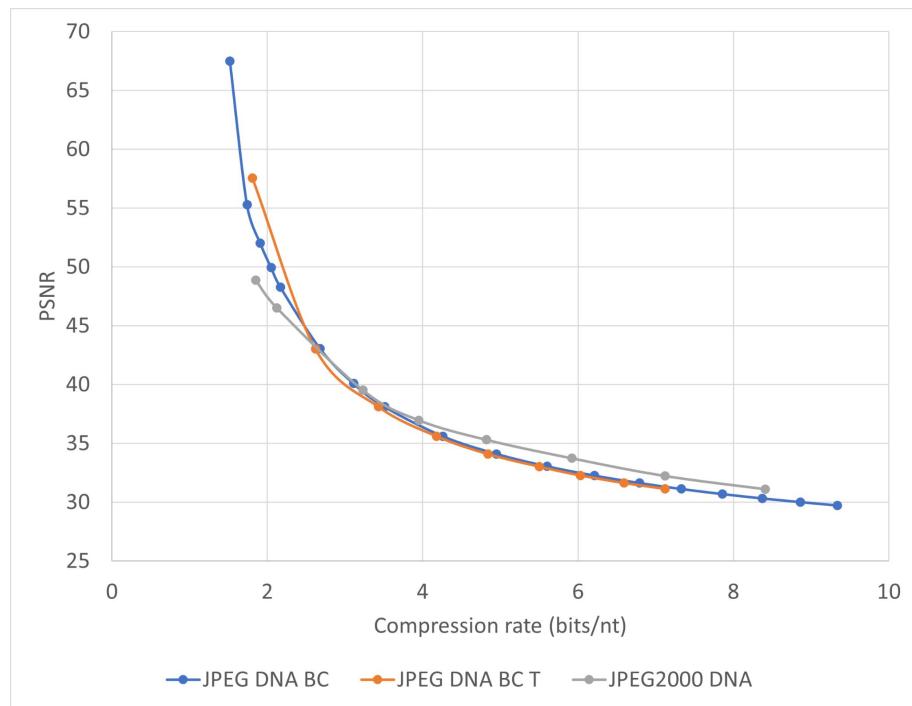


Fig: Adaptation to DNA of the JPEG2000 codec

# JPEG2000 DNA - Results

- Tested across the kodak dataset
- On the right, an example of encoding one image of the kodak dataset (kodim7) using the JPEG DNA 2000 codec
- Performance mostly similar with the original JPEG DNA BC software



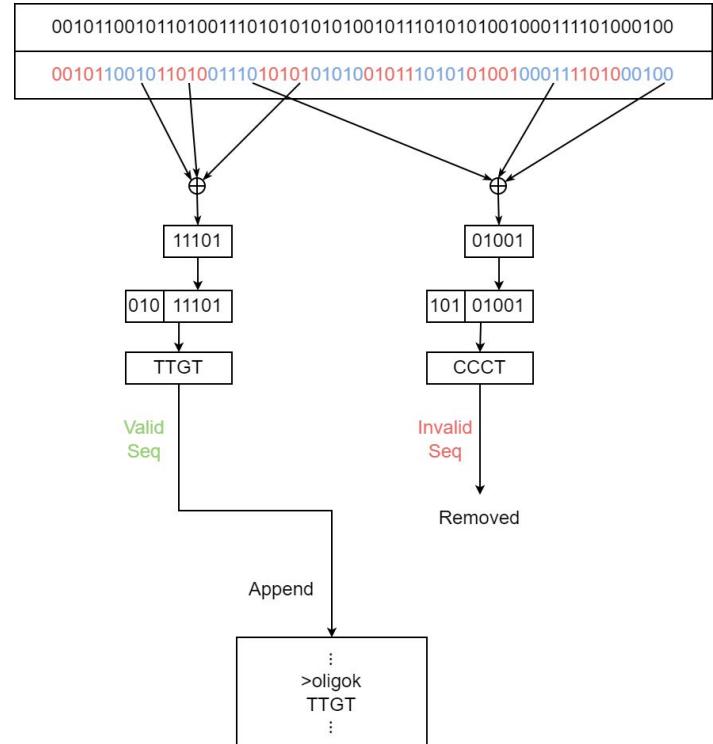
Kodak dataset, weblink: <https://r0k.us/graphics/kodak/>

# Examples of DNA Channel Coders

JPEG DNA VM

# DNA Fountain Codes - Raptor Code

- **Cut** the memory into bytes
- Randomly **Select and sum** a fixed number of these bytes
- Seed and **encode** into DNA
- **Repeat** the bytes **selection, sum** and **encoding** until all bytes are encoded



**Fig:** A DNA adapted fountain code

Y. Erlich and D. Zielinski, “DNA fountain enables a robust and efficient storage architecture”  
Science, vol. 355, no. 6328, pp.950–954, 2017

# Fountain code adapted to DNA

- Fountain code
- Encode the XORed chunks into DNA with the following table:

Input bits	DNA code
00	A
01	T
10	C
11	G

# Selection of the oligos

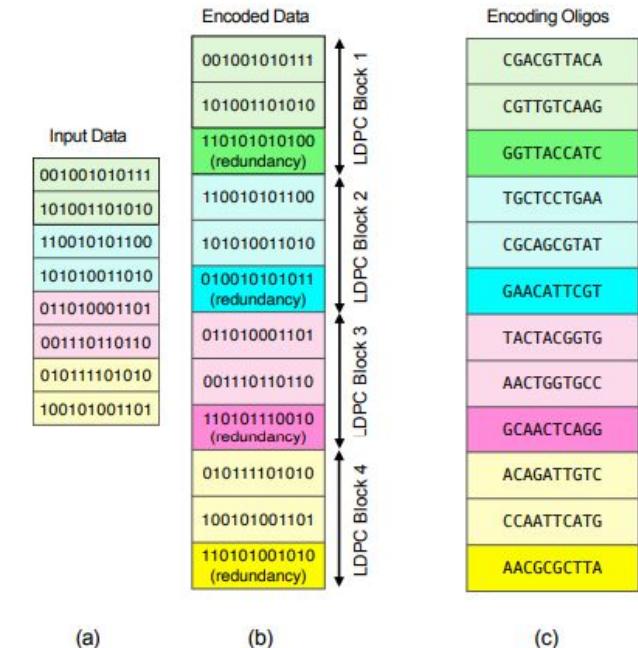
- Code is **not constrained**
- Some generated oligos will not respect the constraints
- **Remove all the oligos** that don't respect the constraints
- Check that there is still enough **redundancy**, otherwise:
  - Start the whole process all over
  - Change the seed for the random selection of chunks

# Examples of DNA Channel Coders

CMOSS

# CMOSS - Encoding in columns

- Data is first organized in columns
- Each line in the column has a set number of bits
- Lines are grouped in blocks
- Redundancy is introduced (LDPC block)
- Each line is encoded into DNA using a motif



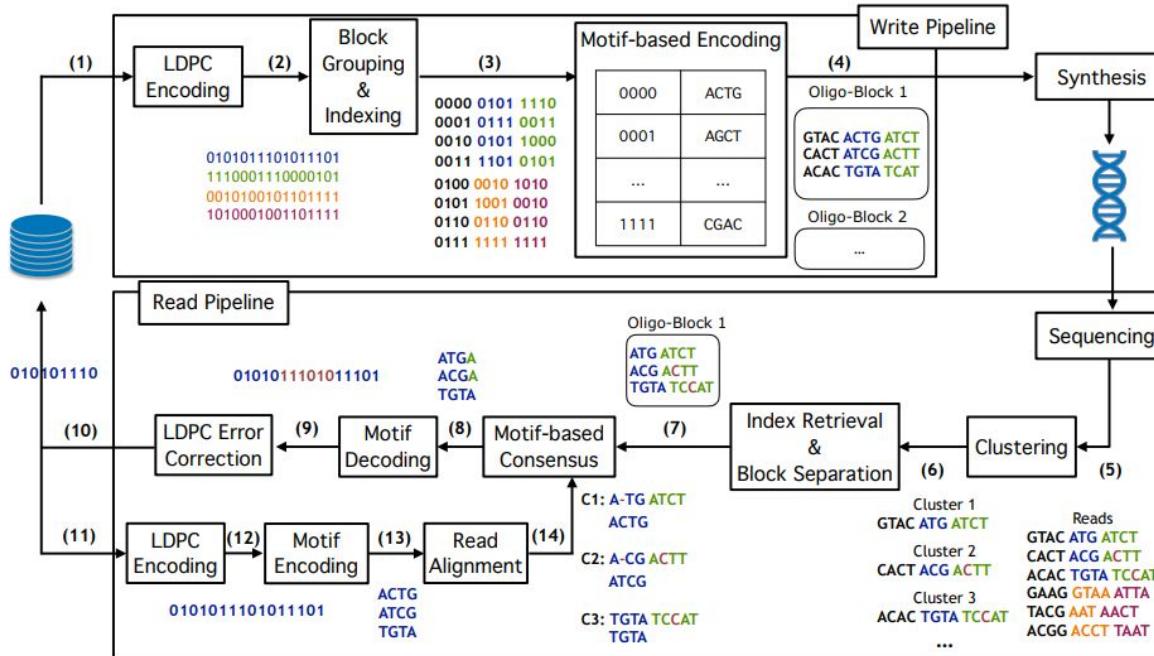
# CMOSS - A motif-based coding system

- Preconstructed set of motifs that can be used to encode data
- Translation table
- Motifs are synthesized in large numbers
- Ligated (concatenated) into larger oligos

# CMOSS - A consensus-driven coding system

- PCR allows the cheap copy of DNA molecules
- Easier to decode noised data when you have a lot of copies of it
  - Try to sequence all of the molecules
  - Operate a clusterization and consensus (merge the data from all the copies)
- Compute the minimal coverage (average number of copies) necessary to read, to be sure to decode the data

# CMOSS - General workflow



Eugenio Marinelli, Yiqing Yan, Lorenzo Tattini, Virginie Magnone, Pascal Barbry, Raja Appuswamy, "CMOSS: A Reliable, Motif-based Columnar Molecular Storage System", 17th ACM International Systems and Storage Conference

# Examples of DNA Image Coders

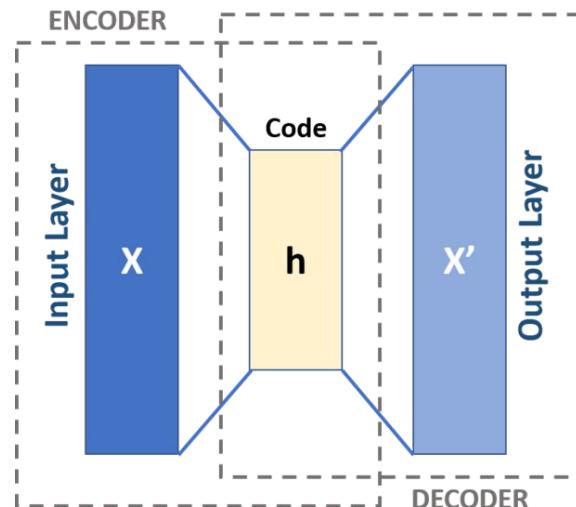
AI-based Image coder (HiDNA)

# Motivations

- Learning-based models such as JPEG AI are very promising
- AI-based methods can be used to adapt to noise

# Principle - Synthesis Model

- The model learns to represent an image into a latent space (encoder side)
- Reconstruct the same image from the latent space (decoder side)
- Latent space is a tensor of fixed dimensions



# Synthesis model - Training phase

A loss based on the minimization of the **rate** of the latent space and the **reconstruction quality** of the image:

$$L = D(I, \hat{I}) + \lambda \times H(y)$$

where:

- $I$ : Input image
- $\hat{I}$ : Reconstructed image
- $y$ : Latent space
- $D$ : Distortion metric
- $H$ : Entropy

# Principle - Latent Space Coding

- Fully connected neural network (ARM Model)
- Learns the Probability Density Function of each element of the latent space, depending on its context
- The PDF is used to instantiate an arithmetic, binary entropy coder, associated with a DNA adapted coder

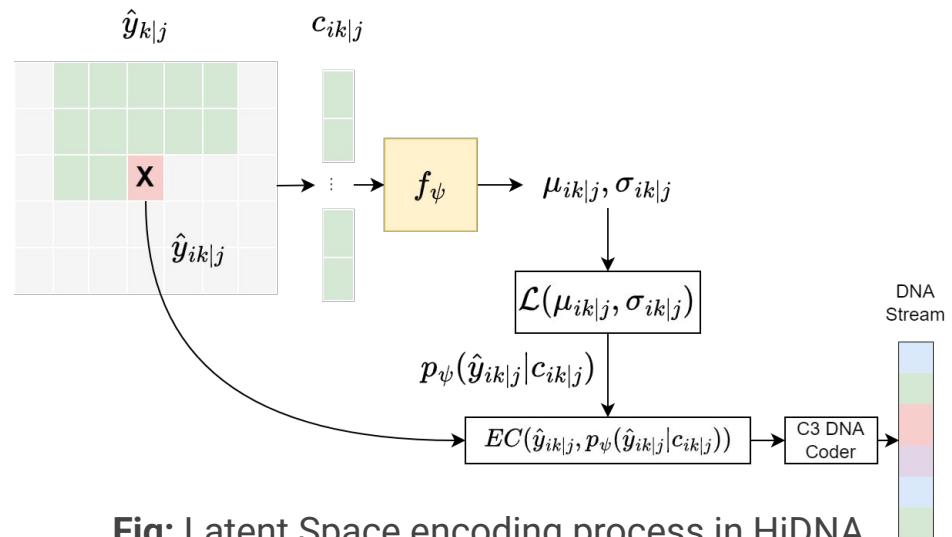
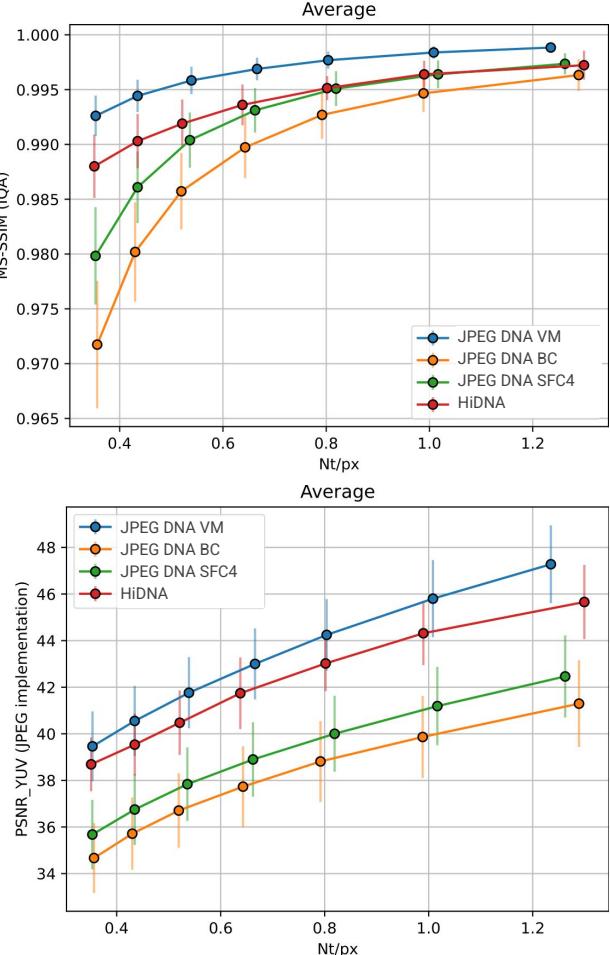


Fig: Latent Space encoding process in HiDNA

# Results

- HiDNA overperforms all other state of the art source coders
- Only the JPEG DNA VM ([open loop](#) adaptation of JPEG XL to DNA) performs better



# Conclusion

- A series of coding softwares have been adapted to DNA data storage or implemented
  - For images (source coders and joint source/channel coders):
    - JPEG DNA SFC4, JPEG 2000 DNA, HiDNA
  - For any kind of data (channel coders):
    - C3, SFC4, Raptor Code
- Fairly new field of research -> Still opportunities for improvement in several fields (coding theory, information theory)

# References

- PEPR MoleculArxiv (French Gvt - ANR)
- Molecular-Scale Data Storage and Archiving (USA - IARPA)
- DNA Data Storage Alliance (SNIA Technology Groups)
- Companies and labs: Wyss Institute, Twist Bioscience, Catalog DNA, Biomemory, PearCode

# Thank you !

[xavier.pic@eurecom.fr](mailto:xavier.pic@eurecom.fr)  
[xavpic.github.io](https://xavpic.github.io)

EURECOM - Data Science

# References

- Y. Erlich and D. Zielinski, "DNA fountain enables a robust and efficient storage architecture" *Science*, vol. 355, no. 6328, pp.950–954, 2017
- George M. Church, Yuan Gao, and Sriram Kosuri, "Next-Generation Digital Information Storage in DNA", *Science*
- N. Goldman, P. Bertone, and S. Chen, "Towards practical, high-capacity, low-maintenance information storage in synthesized DNA," *Nature*, 2013
- A. Banerjee, A. Wachter-Zeh and E. Yaakobi, "Insertion and deletion correction in polymer-based data storage", *IEEE Trans. Inf. Theory*
- R. Gabrys, S. Pattabiraman and O. Milenkovic, "Mass error-correction codes for polymer-based data storage", *IEEE Int. Symp. Inf. Theory (ISIT)*
- R. N. Grass, R. Heckel, M. Puddu, D. Paunescu and W. J. Stark, "Robust chemical preservation of digital information on DNA in silica with error-correcting codes", *Angew. Chem. Int. Ed.*
- M. Dimopoulou, E. Gil San Antonio, M. Antonini, "A JPEG-based image coding solution for data storage on DNA", *EUSIPCO*, 2021
- Davi Lazzarotto, Jorge Encinas Ramos, Michela Testolina, Touradj Ebrahimi, "Storing images and point clouds on DNA support with fountain codes", *Applications of Digital Image Processing XLVII*
- Eugenio Marinelli, Yiqing Yan, Lorenzo Tattini, Virginie Magnone, Pascal Barbry, Raja Appuswamy, "CMOSS: A Reliable, Motif-based Columnar Molecular Storage System", 17th ACM International Systems and Storage Conference
- X. Pic and M. Antonini, "A constrained shannon-fano entropy coder for image storage in synthetic DNA", *EUSIPCO* 2022
- X. Pic, M. Dimopoulou, E. Gil San Antonio and M. Antonini, "MQ-Coder inspired Arithmetic Coder for Synthetic DNA data storage", *ICIP* 2023
- T.H. Le, X. Pic, J. Mateos and M. Antonini, "Implicit Neural Multiple Description for DNA-based data storage", *ICASSP* 2023