Deciphering DNA using AI

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University of Maryland, Johns Hopkins University

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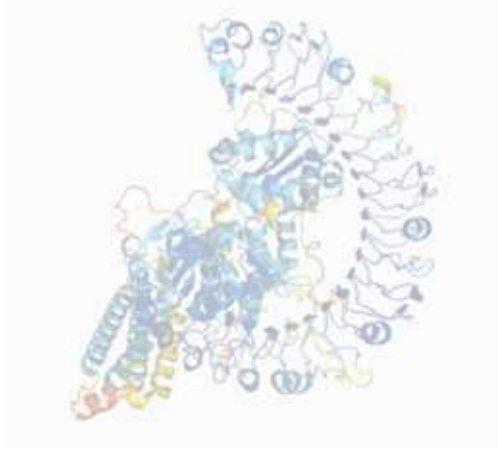

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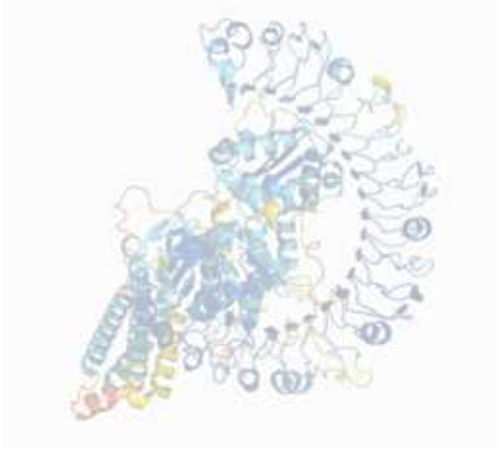
Motivation:

- Genomic Medicine
- Basic biology: evolution



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Our goal

Identify Protein-Coding Regions in DNA

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Our goal

Identify Protein-Coding Regions in DNA

Our strategy

- Generate candidates from evidence
- Use binary classification to filter unreliable ones

DNA

Genes are 50% of DNA

Coding sequence is 2% of genes

gene gene

…**ATGAC**GTCAGA……GATATCAG**ATAGATCA**……**AGCATCATA**GTGACATA……AG**CATATAGCGAT**…

- **sequence of 4 symbols** {**A**, **C**, **G**, **T**}
- carrying the **genome information** (proteins, RNA, regulation, etc.)

For human genomes…

- The whole sequence is about **3 billion** bases (3GB text)
- About 50% are **gene** regions
- Roughly 2% of the gene is protein-coding

DNA

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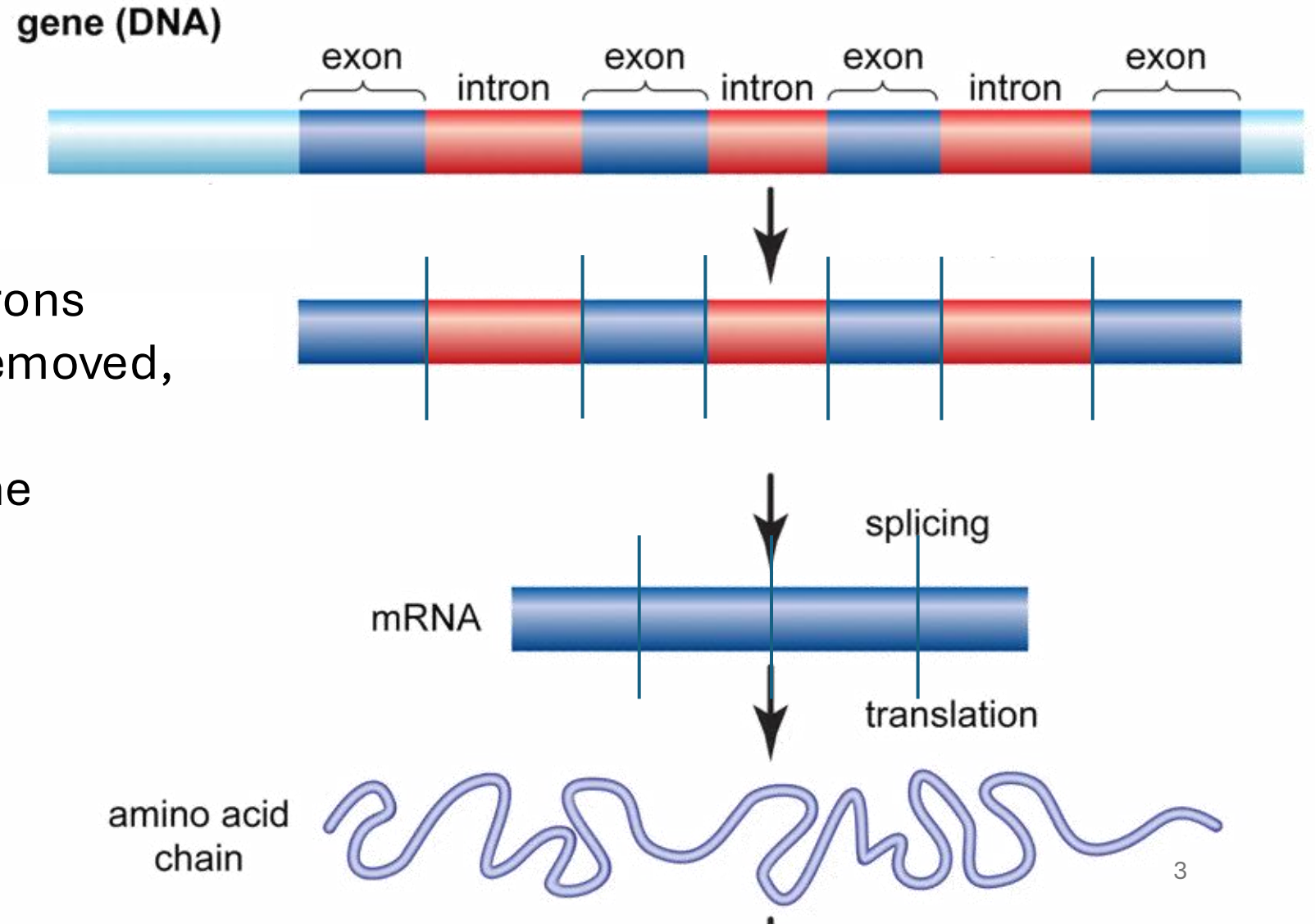
Biological Process: Splicing

- Genes contain exons and introns
- During splicing, introns are removed, and exons are joined to mRNA
- What we want to identify is the boundary in the genome

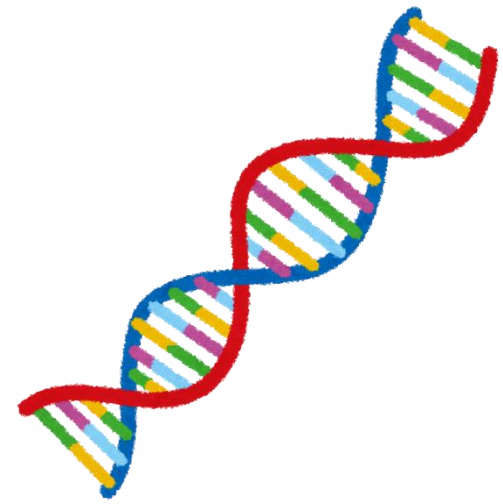


Problem:
Identify Splice Boundaries from DNA

Input

Output

...ATGACGTCAGAGATATCA
GATAGATCAAGCACATAGT
GACATAAGCATAGTGACAT
AAGCATATCATATTCATAG
TGACATAAGCATATAGCGA
T...



Splicing Machinery

GTACGTCAGAGATATCA
GATAGAG | GTGACATAAG
CATAGTGACATAAGCATAT
CATATTCATAG | GTACGTC
AGAGATATCAGATAGAG

Problem:
Identify Splice Boundaries from DNA

Input

Output

...ATGACGTCAGAGATATCA
GATAGATCAAGCACATAGT
GACATAAGCATAGTGACAT
AAGCATATCATATTCATAG
TGACATAAGCATATAGCGA
T...

AI

GTACGTCAGAGATATCA
GATAGAG | GTGACATAAG
CATAGTGACATAAGCATAT
CATATTCATAG | GTACGTC
AGAGATATCAGATAGAG

Problem:
Identify Splice Boundaries from DNA

Input

Output

...ATGACGT
GATAGATC
GACATAAC
AAGCATAT
TGACATAA
T...

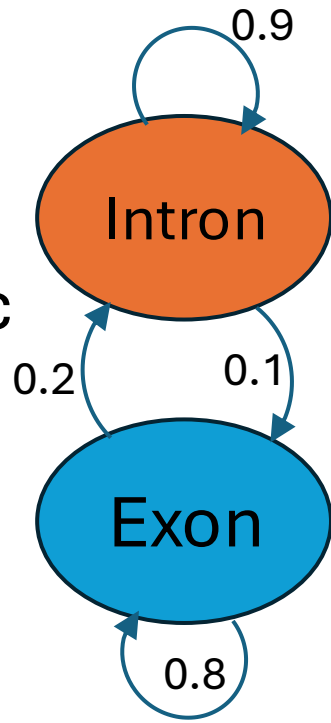
GATATCA
CATAAG
AGCATAT
GTACGTC
TAGAG

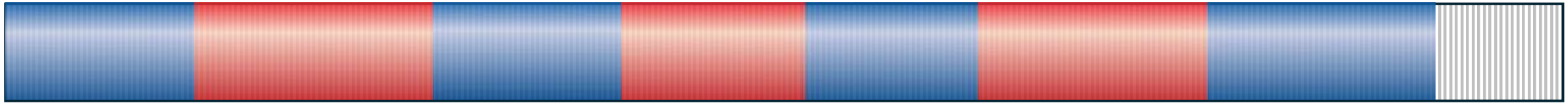
Our task:

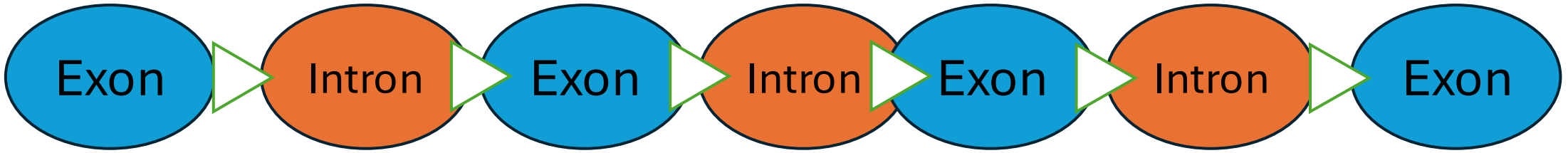
- **Choose the data for training/testing**
- Choose the model architecture
- **Define how to use AI in the pipeline**
- Train AI
- Evaluate AI

One approach:
Predict transition of intron/exon

- Model transitions between Exons and Introns with a stochastic model. (Hidden Markov Model)
- Problem: false positive, stochastic assumption



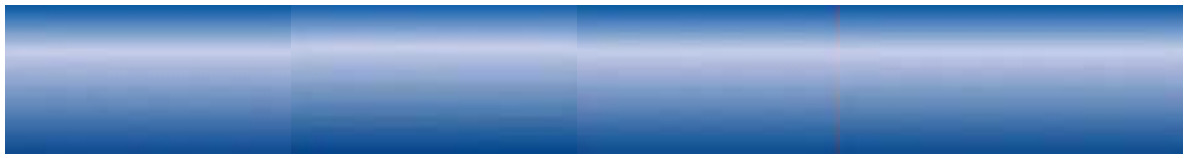




Our approach:
Build candidate transcript → Filter them with AI

- Collect RNA data
- Build transcript by mapping RNA into genome
- Score what the boundary look like (**AI used here!**)
- Score the whole transcript by aggregating boundary scores
- Classify the built transcript **`true/false`**

mRNA

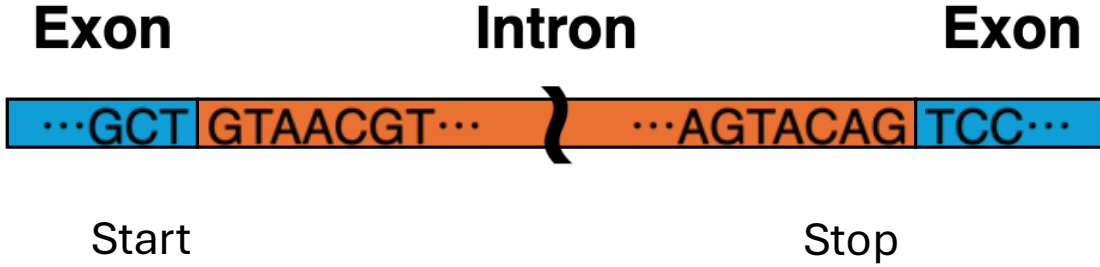


Genome

AI Task:
Binary Classification of Splice Boundaries

Input

- DNA sequence around a boundary around intron
- Fixed-length window of 100 characters



Training data

- Positive examples: “reliable” splice boundaries
- Negative examples: unreliable candidate boundaries

Output

- A score between 0 and 1 indicating confidence

Evaluation is ongoing.
Preliminary results suggest improvement over the previous model.

Summary

- We aim to identify protein-coding regions in DNA
- Instead of scanning the whole genome directly, we use evidence to build candidate transcripts
- We then apply AI to filter unreliable candidates

Take-home message

Reframing the problem can make it more suitable for modern ML models