In the beginning…

DNA

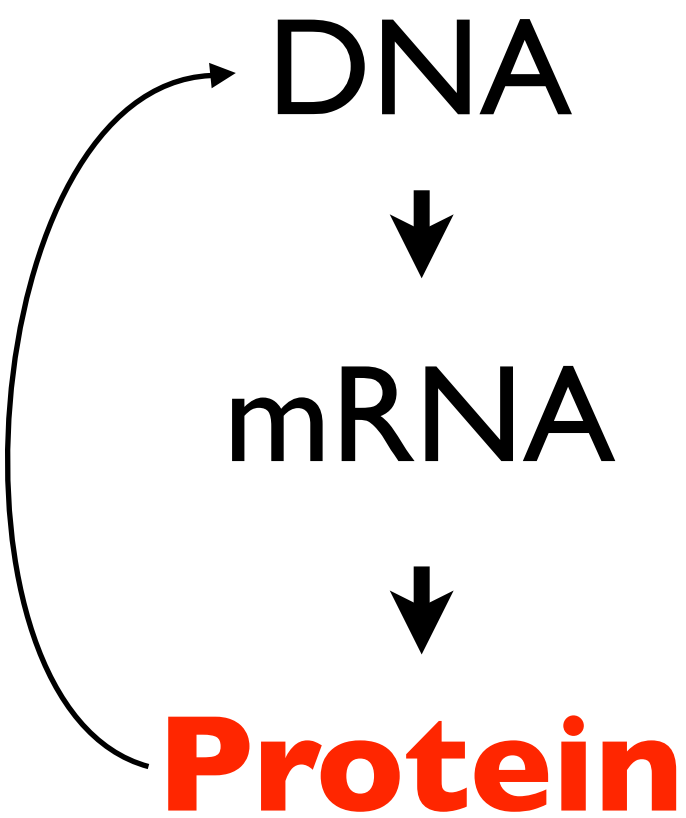
↓

mRNA

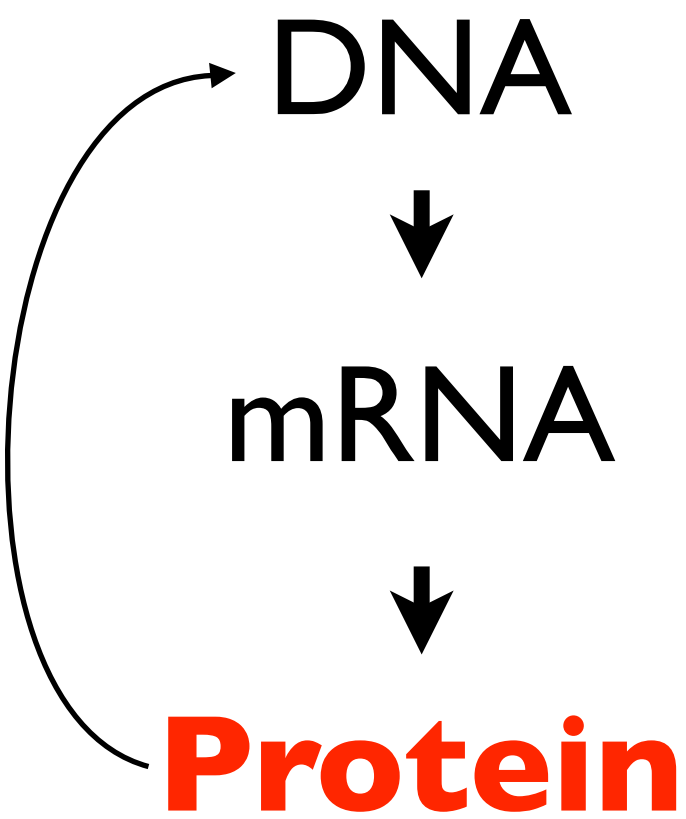
↓

Protein

In the beginning…

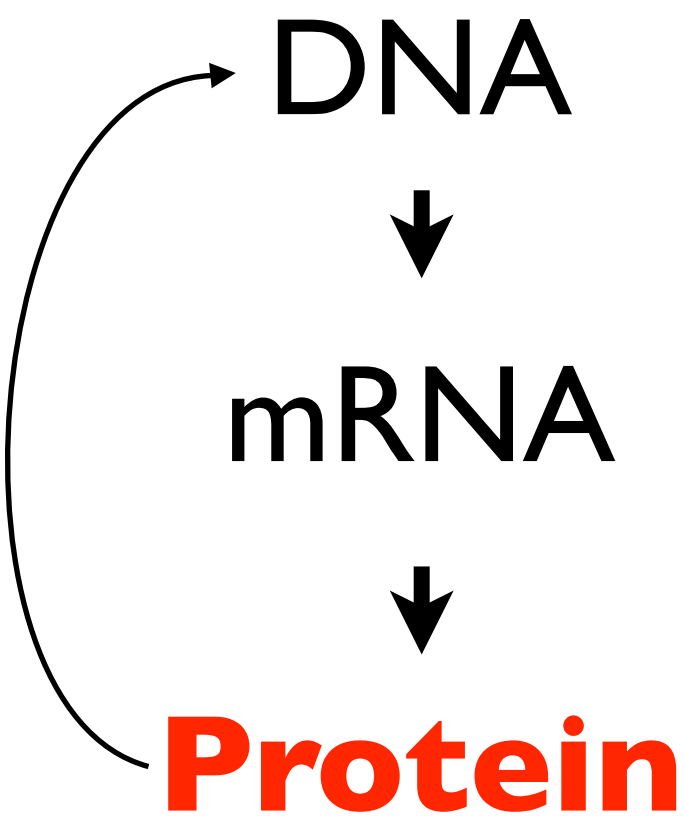


In the beginning…



Archival information storage

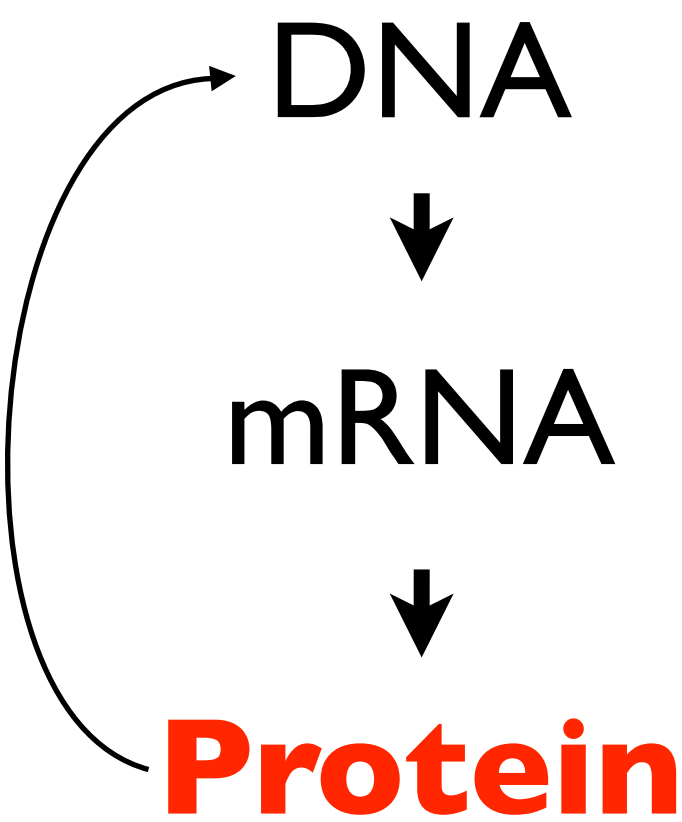
In the beginning…



Archival information storage

Transient information storage

In the beginning…

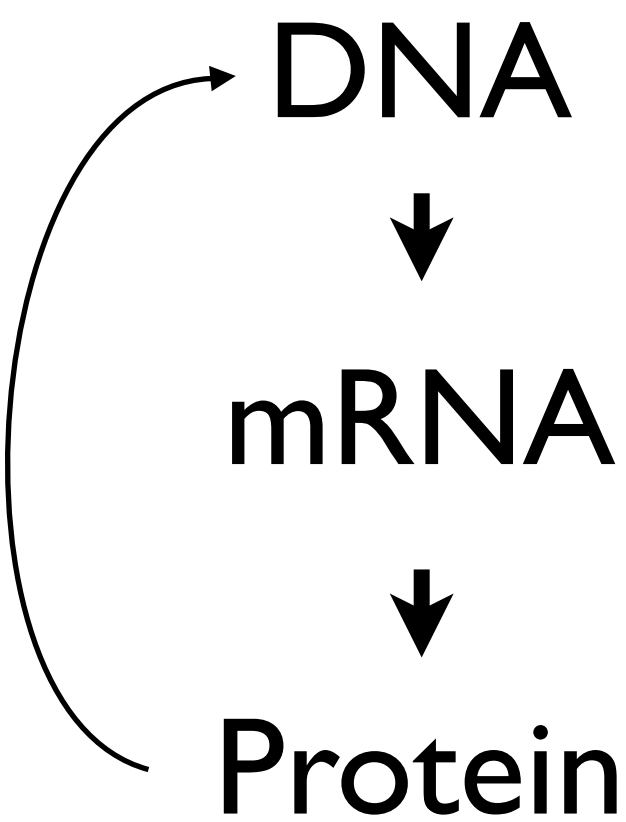


Archival information storage

Transient information storage

Catalysis, structure, regulation, et al.

Chicken & Egg?

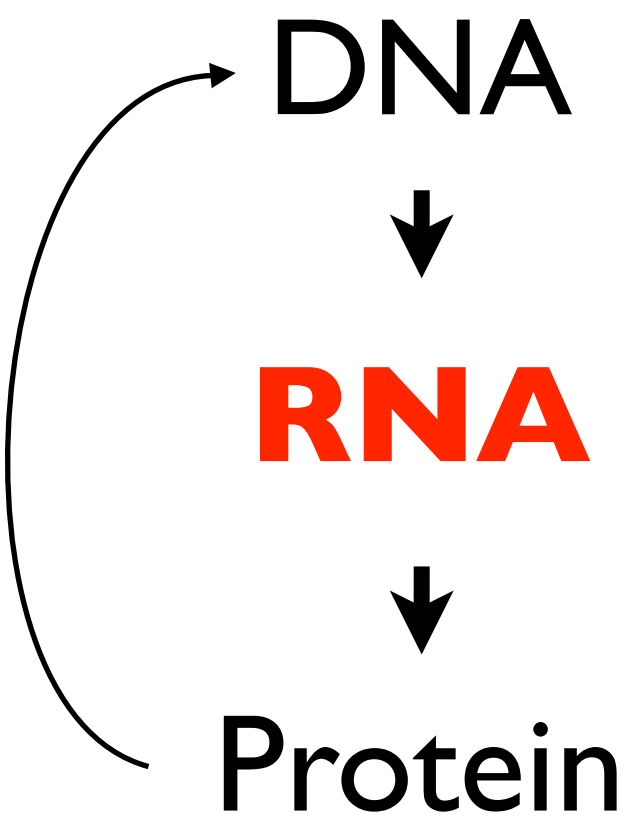


Archival information storage

Transient information storage

Catalysis, structure, regulation, et al.

RNA can do everything



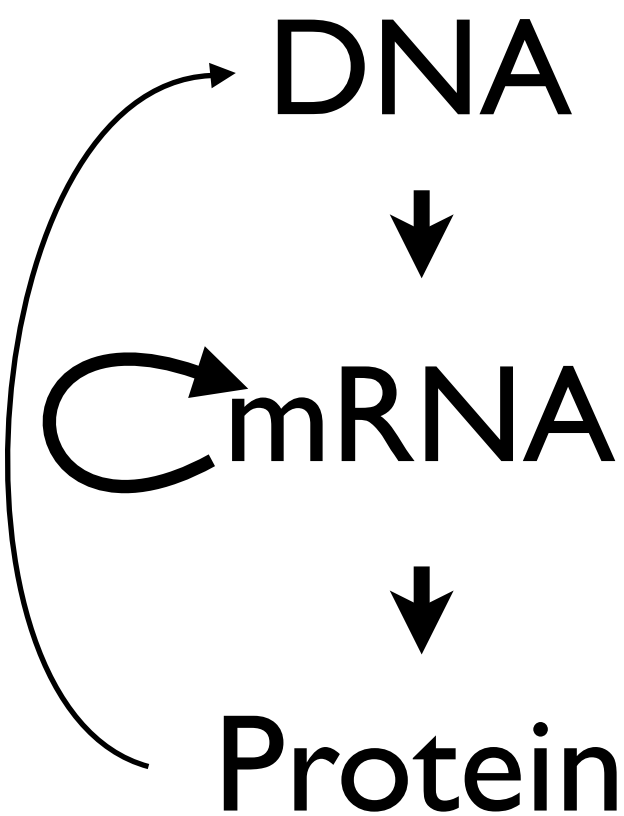
Archival information storage

Transient information storage
Catalysis!

1980-2000

Catalysis, structure, regulation, et al.

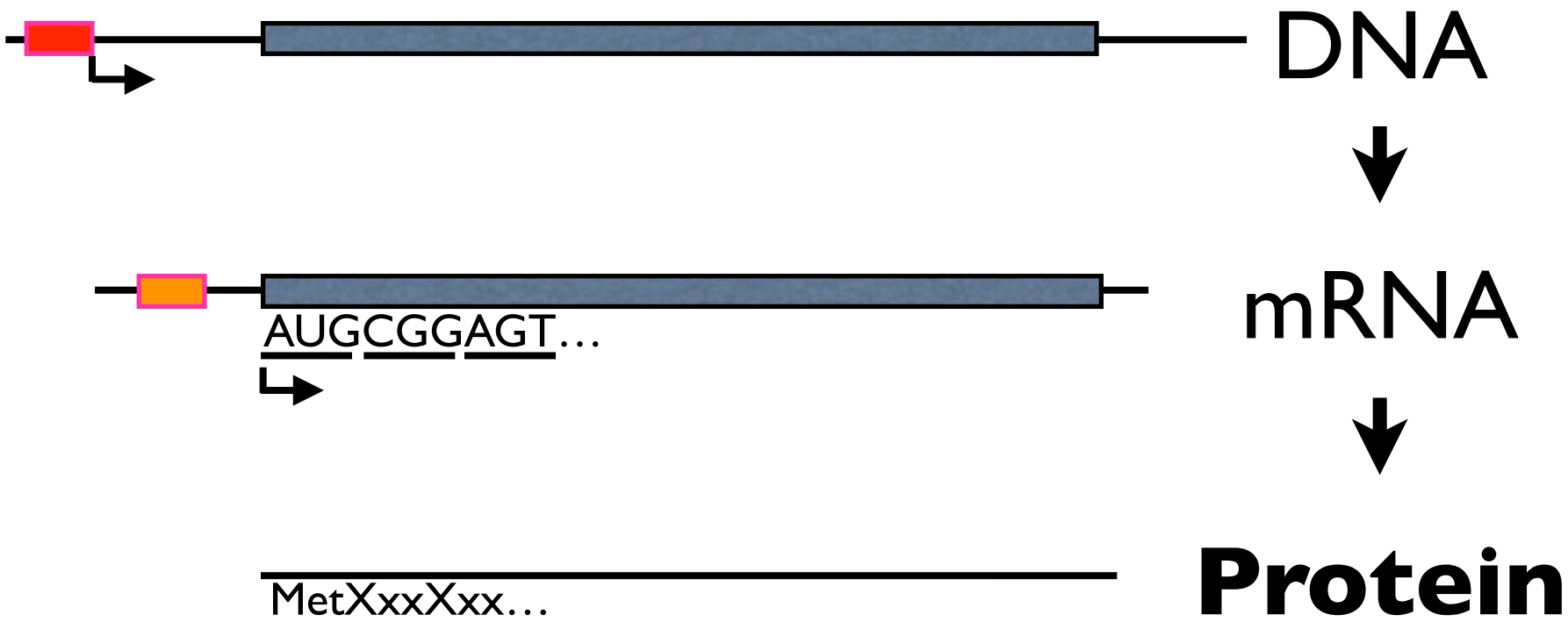
RNA - primordial molecule



So we accepted that RNA was probably the first, primitive do-everything biomolecule.

But **proteins** came along to supplant everything and make the world, evolutionarily, what it is today. All hail the protein!

Seems simple…



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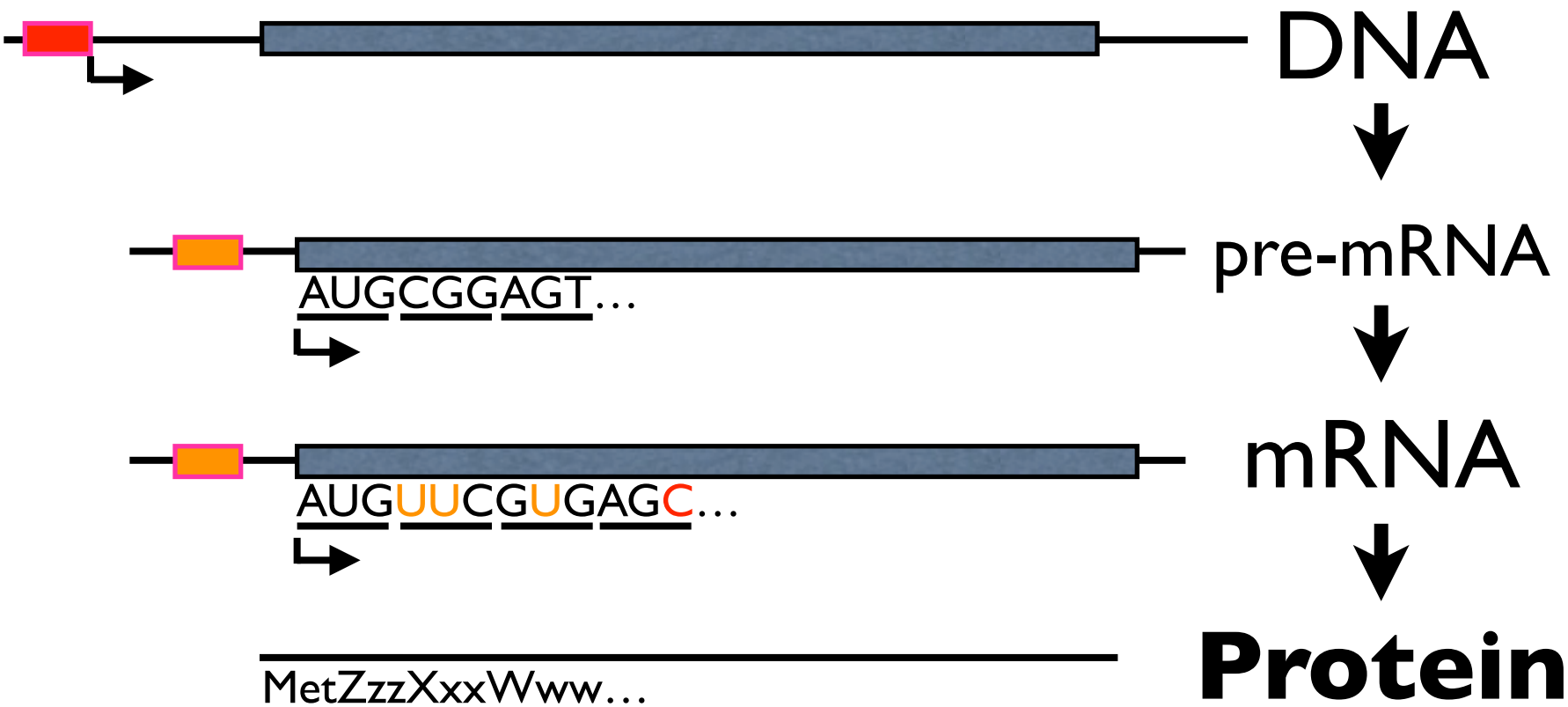
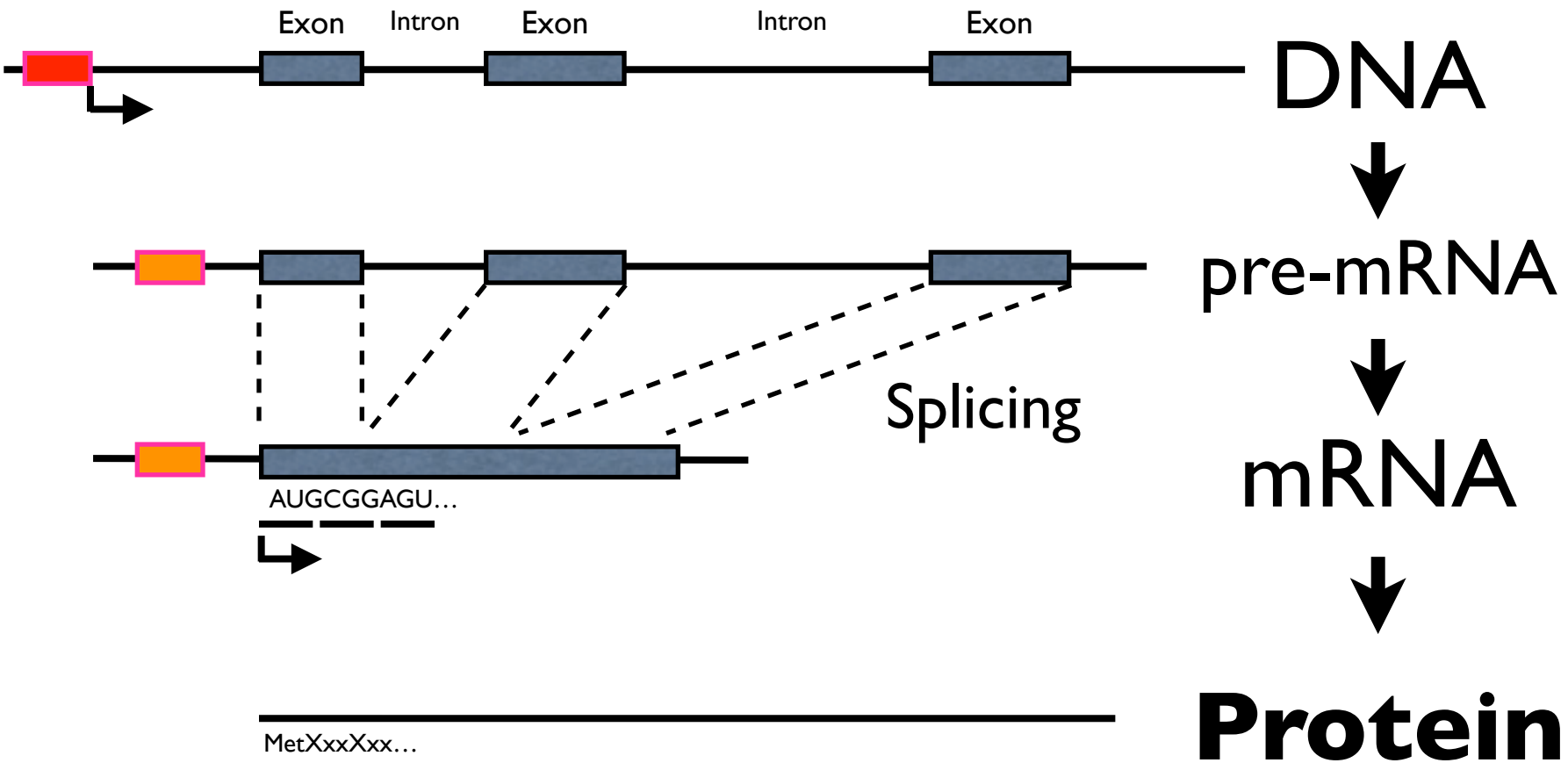
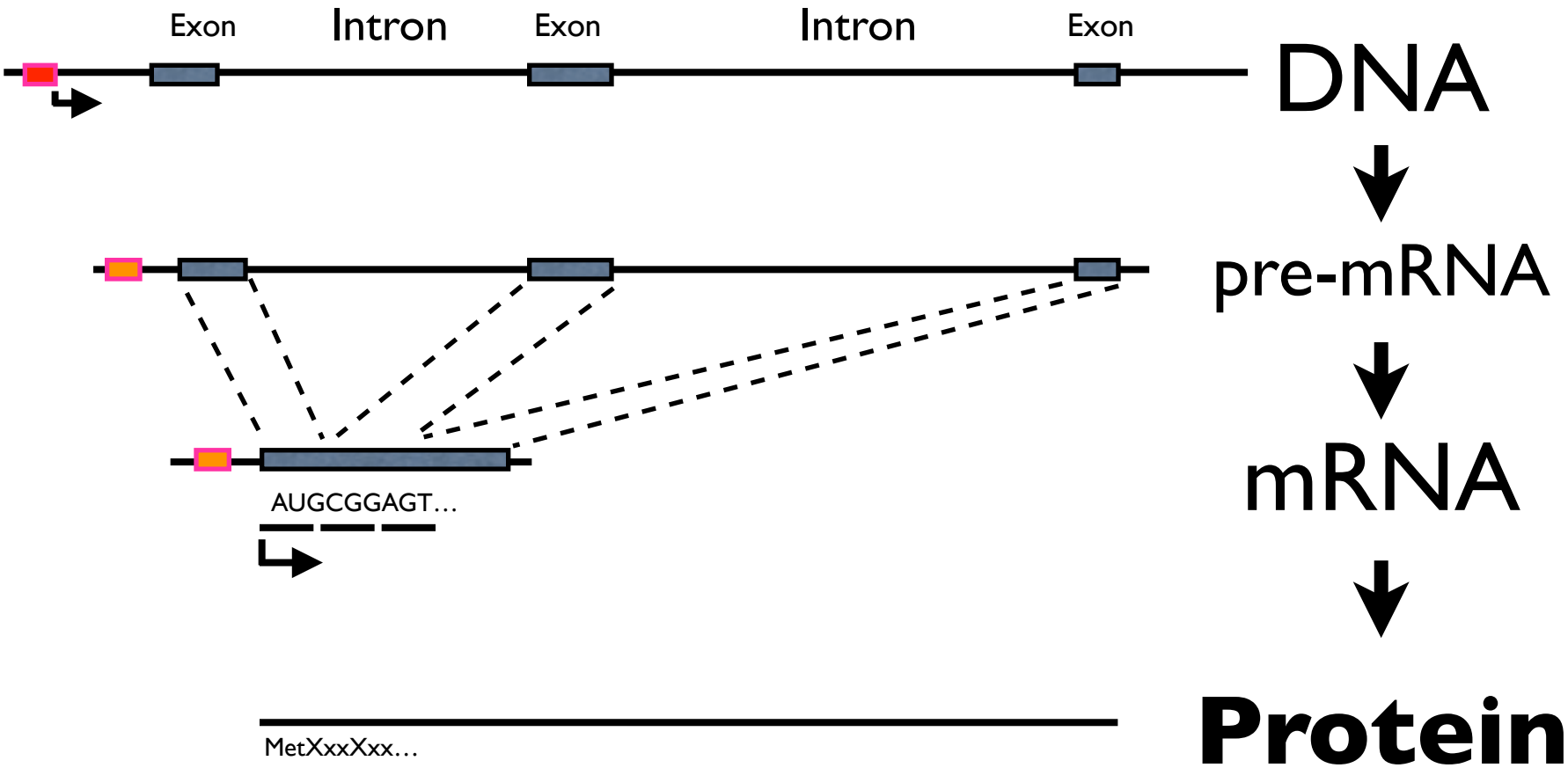


Even more complicated…

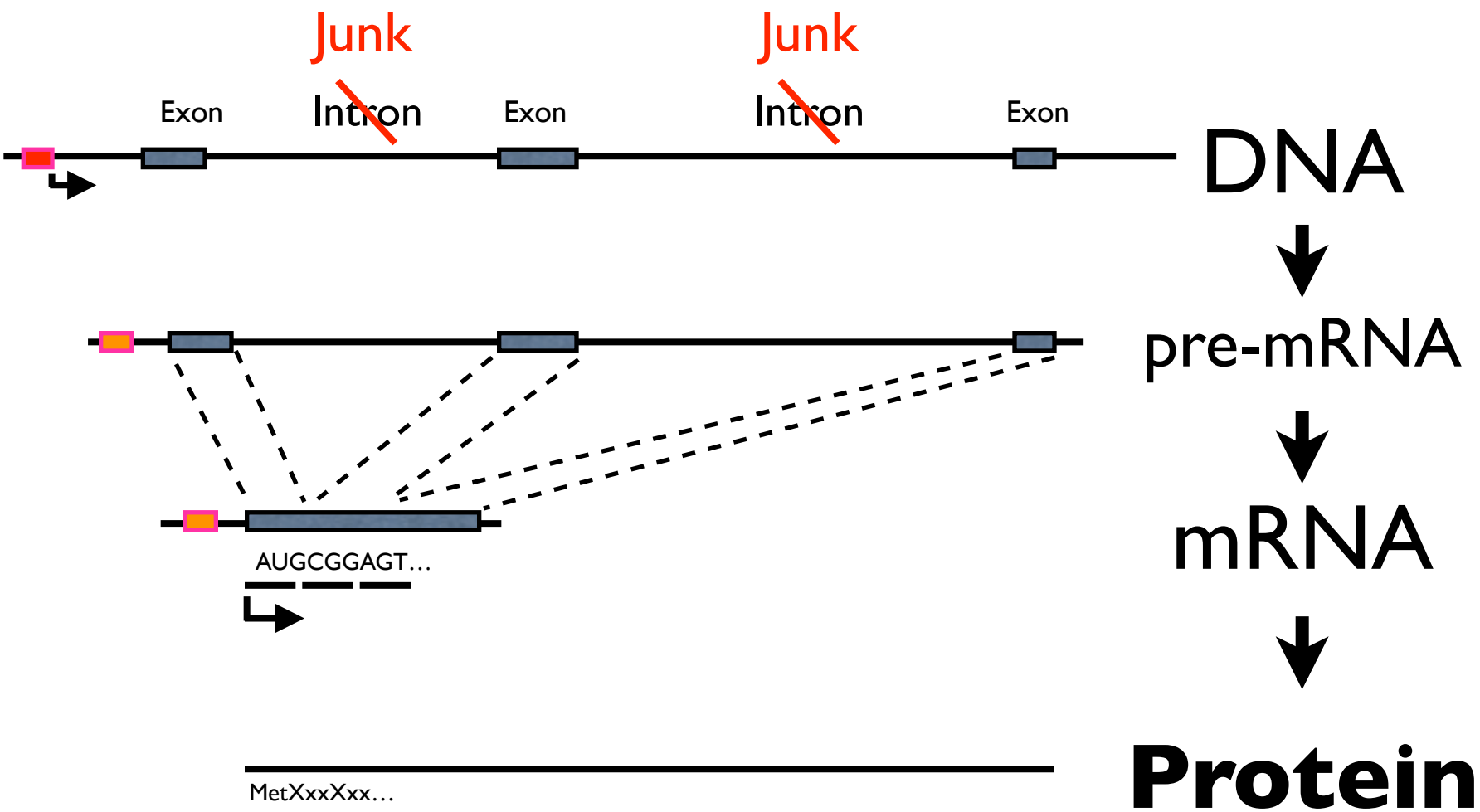


Reality…


Exon
Intron
Exon
Intron
Exon
DNA
pre-mRNA
mRNA
AUGCGGAGT…
MetXxxXxx…
Protein

Reality…

and our perception of it



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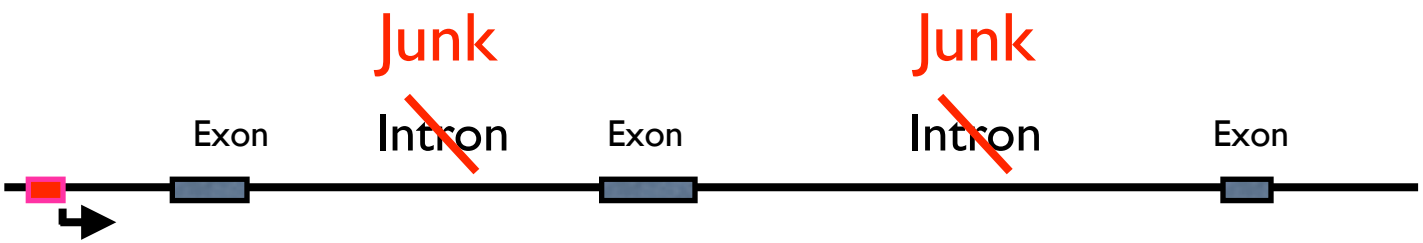

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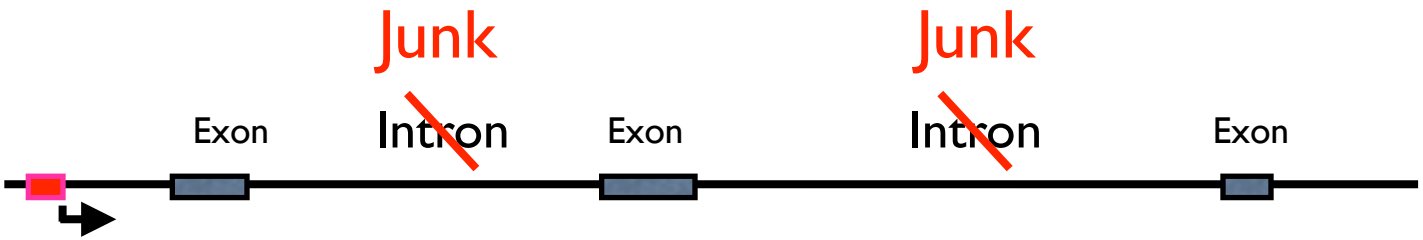

Genome project goals

Identify and characterize the proteins.
What are their structures?
What do they do?
How do they interact?

20th Century View

Polymerases

Kinases

Hydrogenases

Receptors

Oxygenases

Proteases

20th Century View

Kinases

Polymerases

Hydrogenases

Receptors

Oxygenases

Proteases

Nucleic acids → Trash

21st Century News

Genome project

Number of protein-encoding genes in the human genome: 25,000

21st Century News

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Number of protein-encoding genes in the 1,000 cell *C elegans* genome: 19,500

21st Century News

Genome project

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Number of protein-encoding genes in the 1,000 cell *C elegans* genome: 19,500

Number of protein-encoding genes in the corn genome: 40,000

21st Century News

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Number of different proteins: ≫25,000

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21st Century News

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Up to 3/4 of all human genes are subject to alternative editing

21st Century News

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Genome project

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21st Century News

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21st Century News

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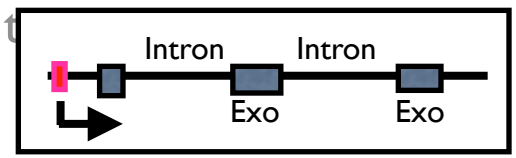

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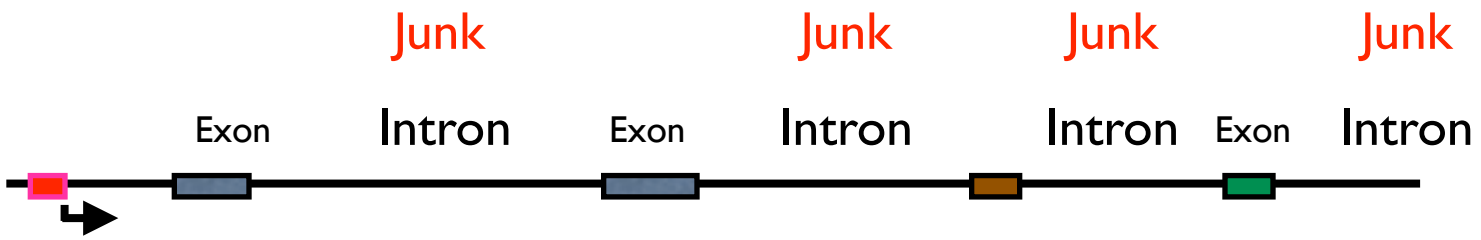
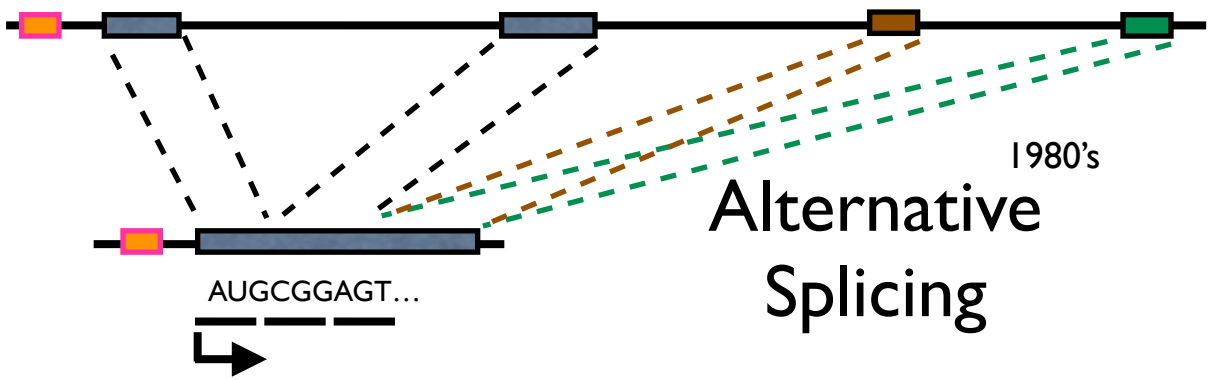
21st Century News



DNA

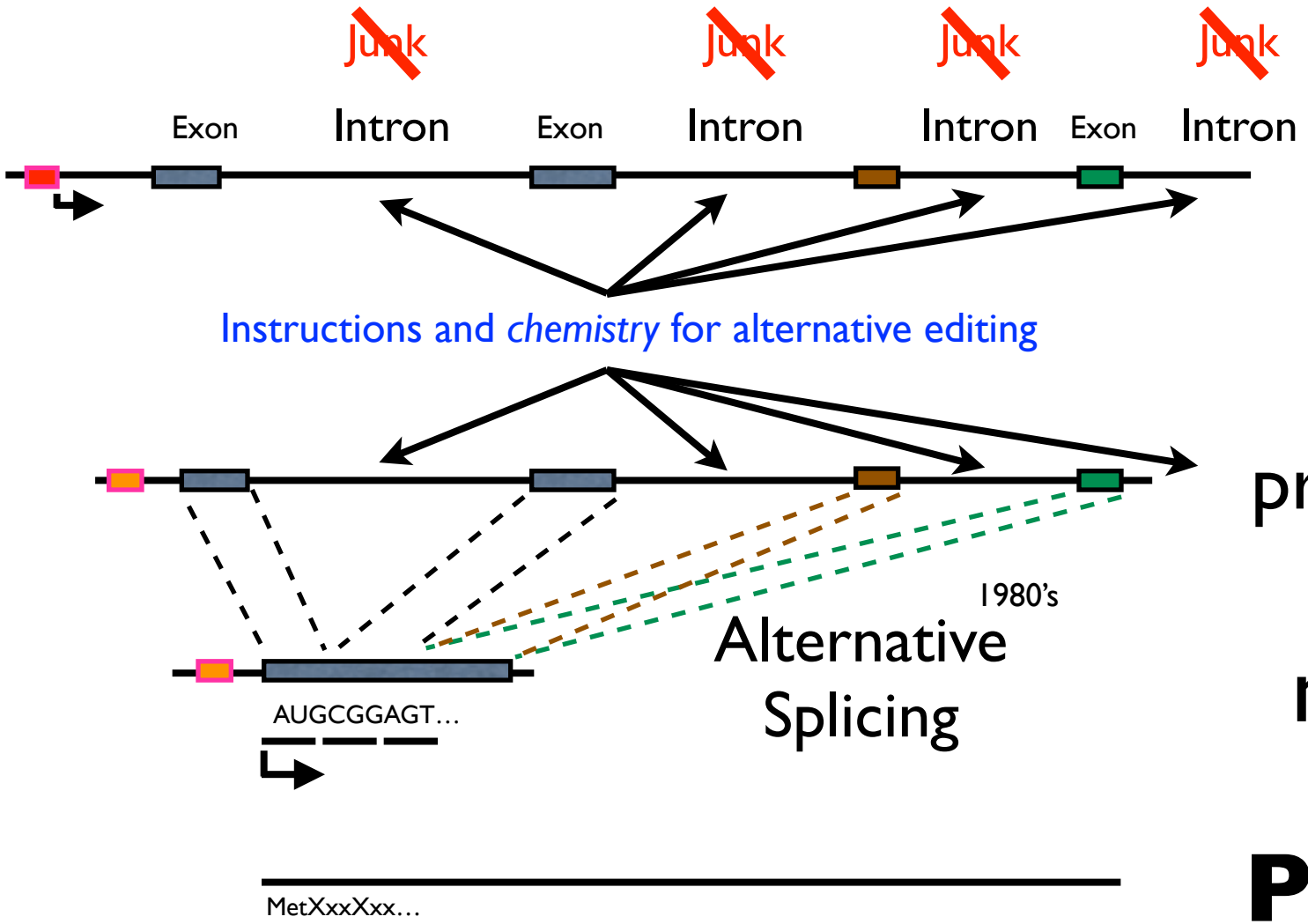


pre-mRNA

mRNA

Protein

21st Century News



DNA

pre-mRNA

mRNA

Protein

Back in the lab…

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With the advent of PCR, nucleic acids have been recognized as extremely powerful combinatorial tools in the test tube

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Can create riboswitches

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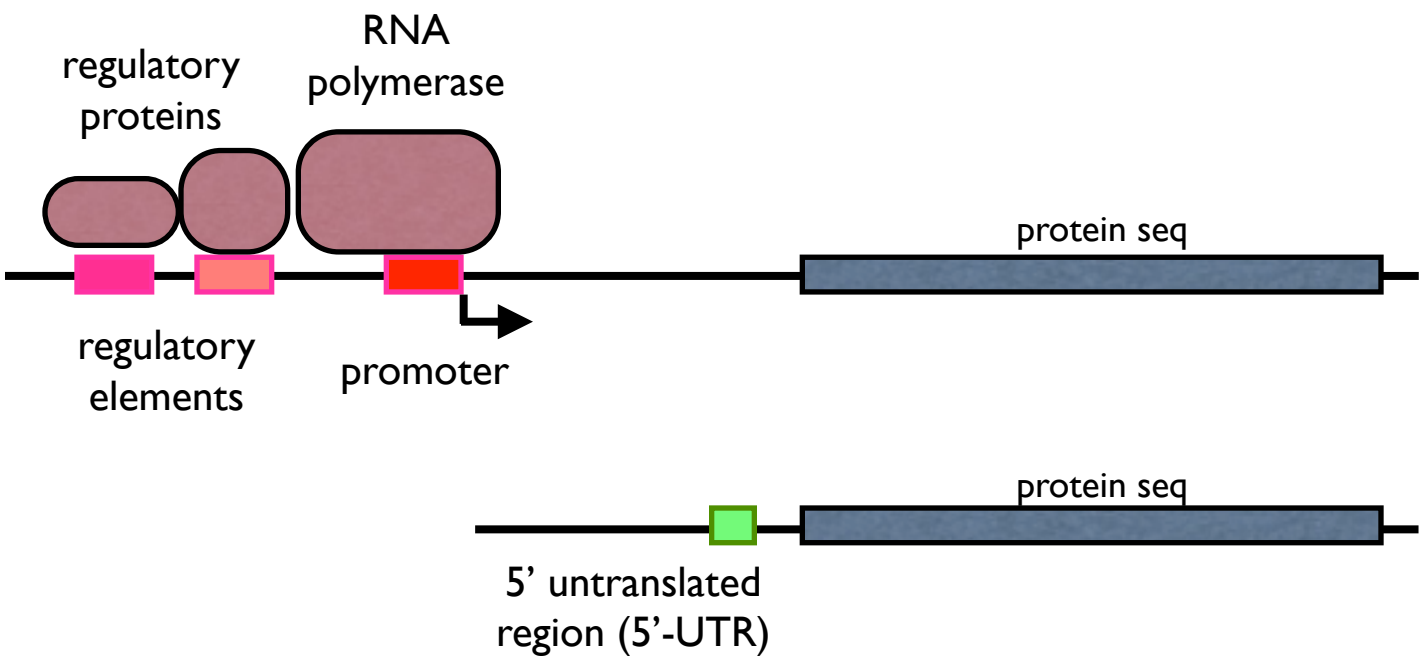
Can create riboswitches

Ron Breaker:
"if it's so easy for us, I'll bet nature exploits this"

More gene regulation



DNA

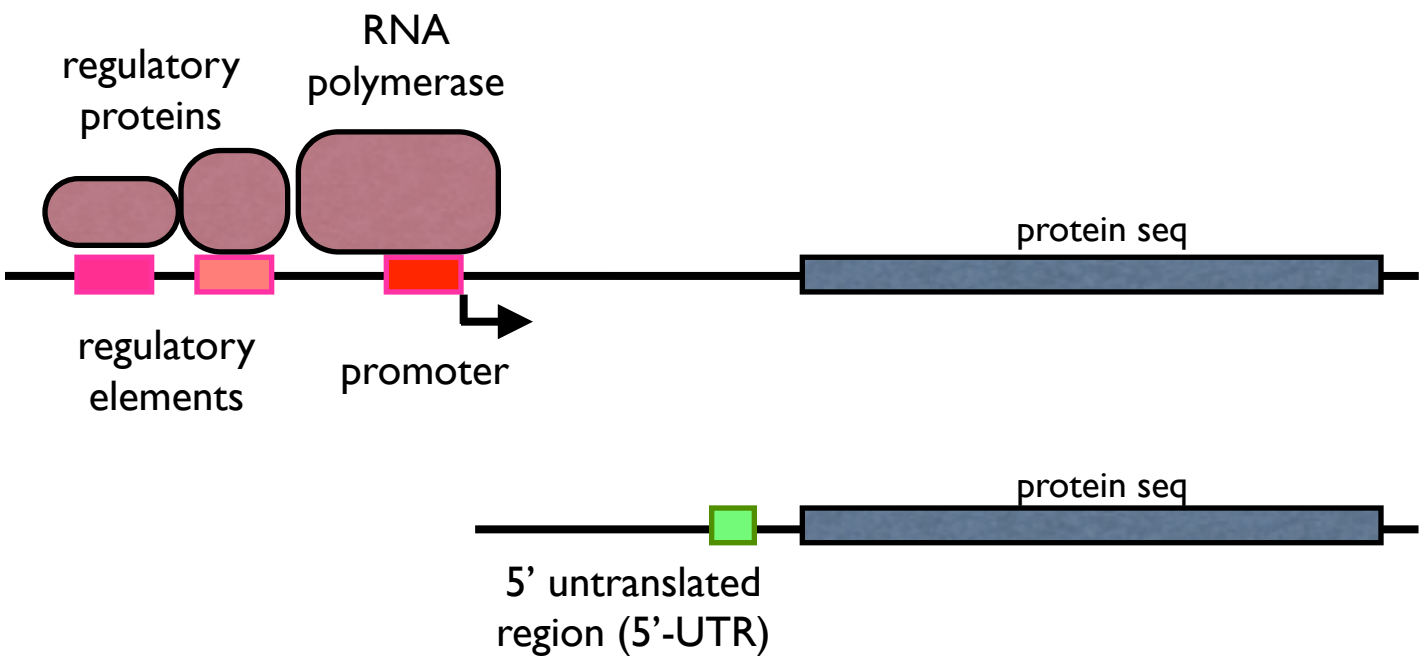
↓

mRNA

↓

Protein

More gene regulation



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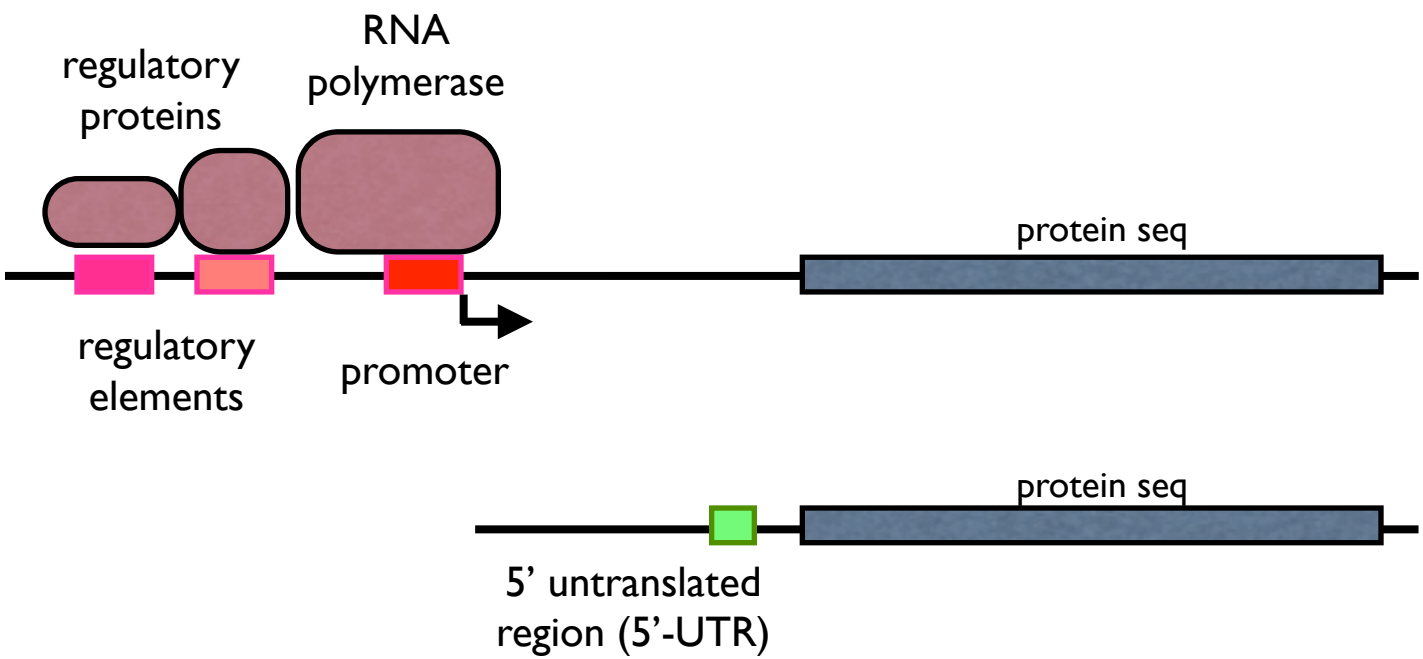
Ron: search for genes with no known protein regulator and which have a highly conserved 5' UTR

More gene regulation



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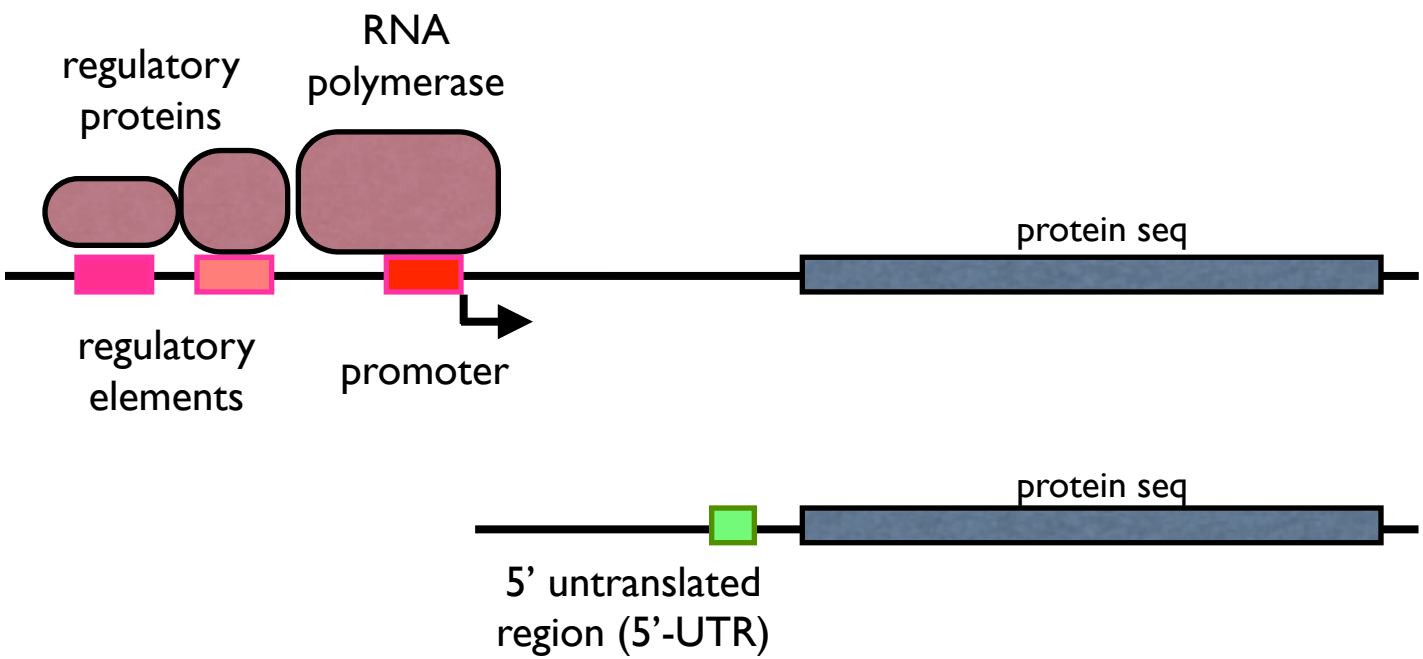
Does RNA from that conserved 5' UTR bind the product or substrate of the encoded enzyme?

More gene regulation



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mRNA

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Protein

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Does RNA from that conserved 5' UTR bind the product or substrate of the encoded enzyme?

2004

↘ One week: a Nature paper!

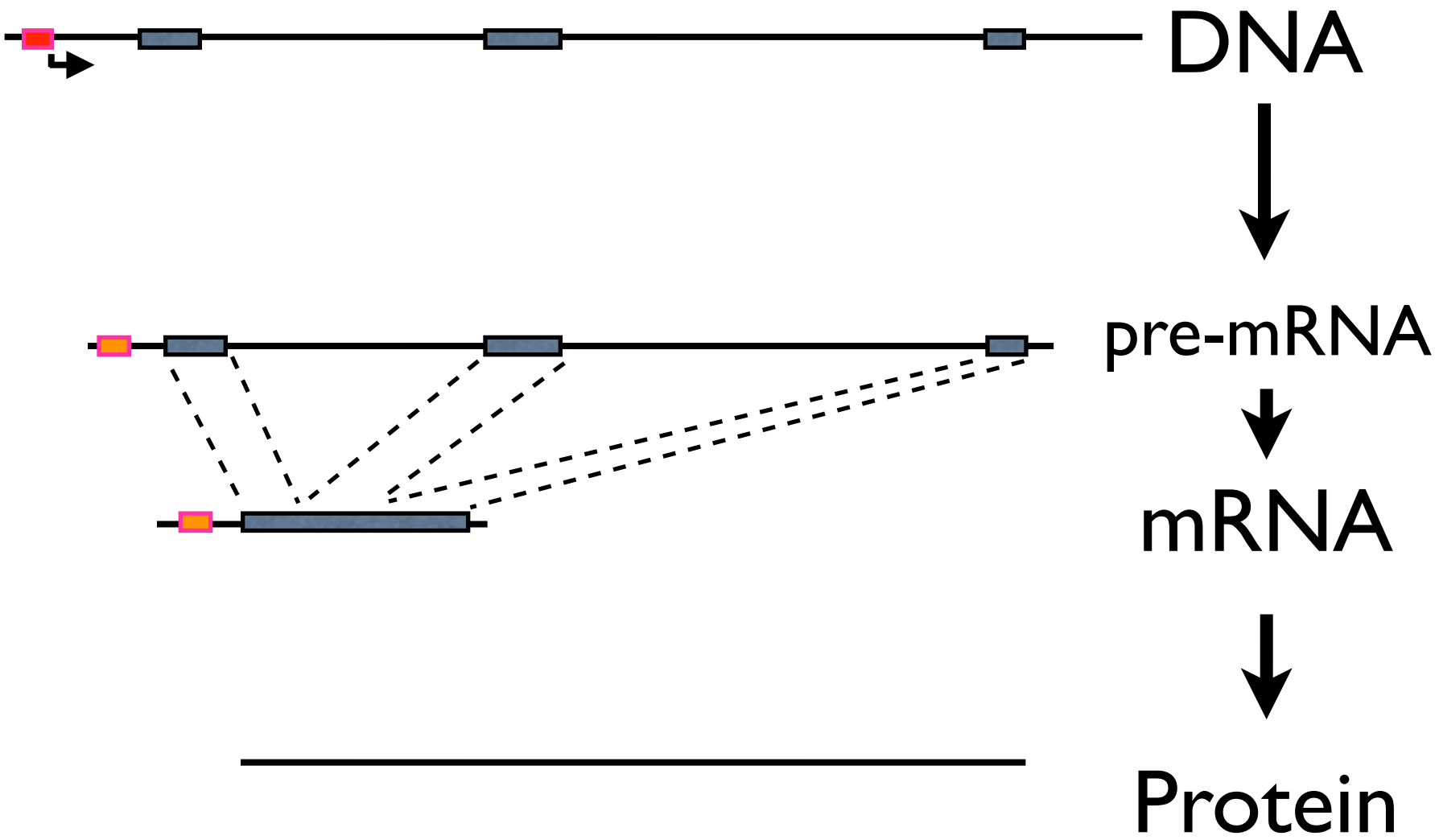
Project Encode (2007)

(More) rewriting of textbooks

June 2007, published in Nature

- Some regions of DNA far from protein-coding genes (extreme "junk?") are nevertheless highly conserved
- Most of both strands of the DNA is transcribed (far beyond that required for protein-coding genes)

21st Century Opportunities

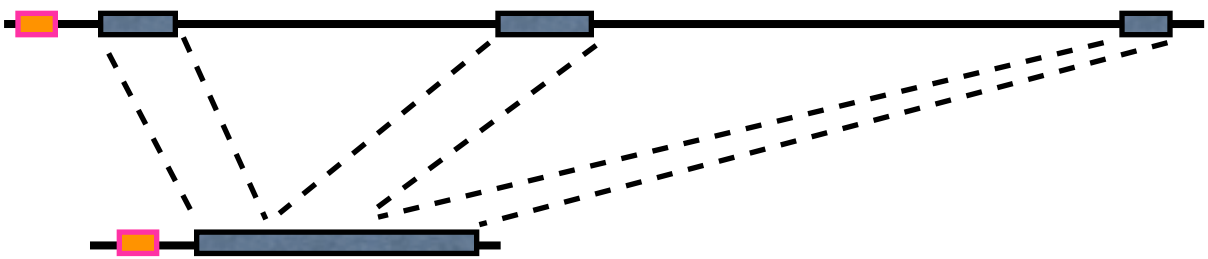


21st Century Opportunities

DNA

early '80s, but…

Alternative splicing



pre-mRNA

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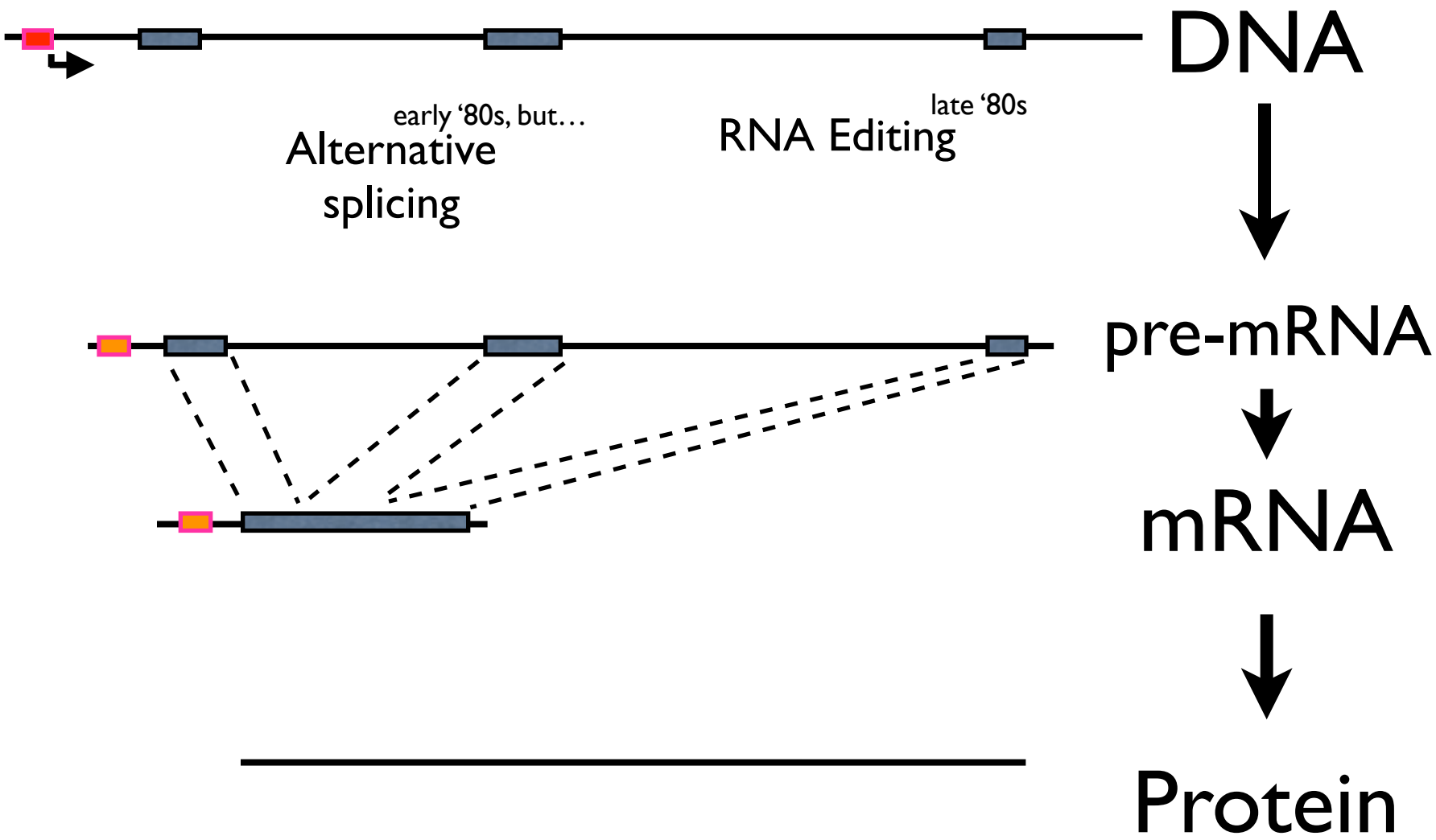
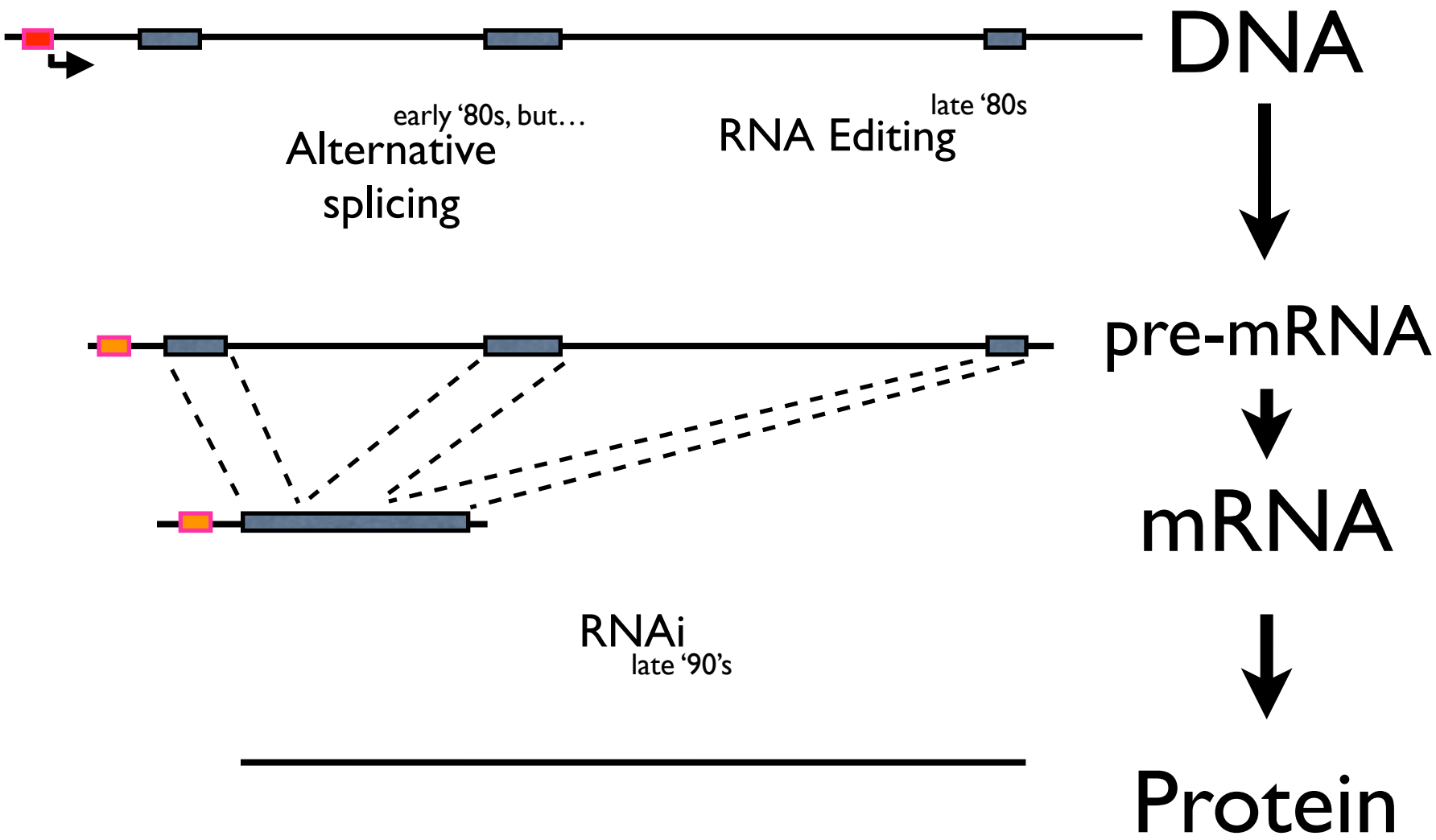
Protein

21st Century Opportunities



21st Century Opportunities



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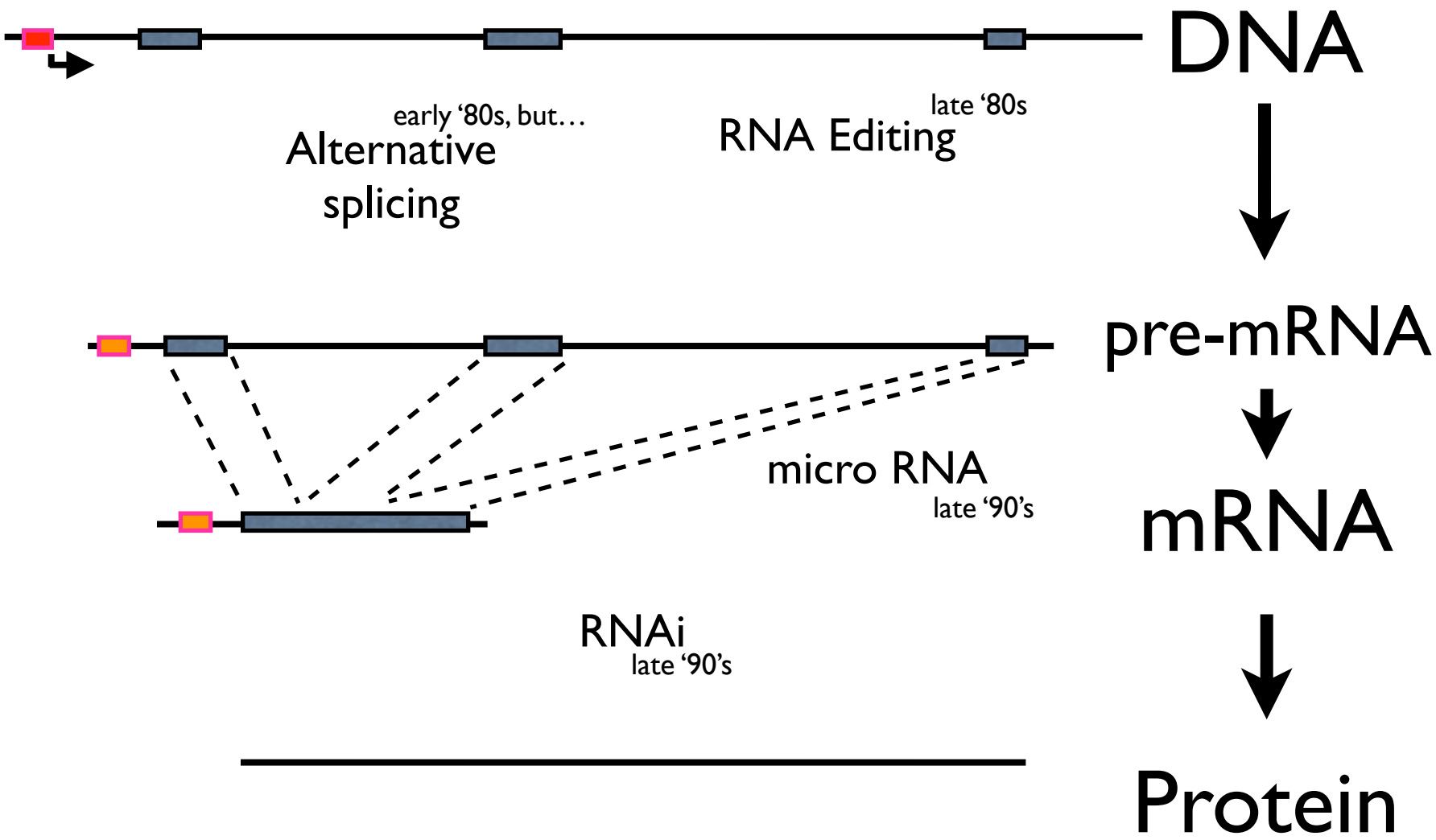

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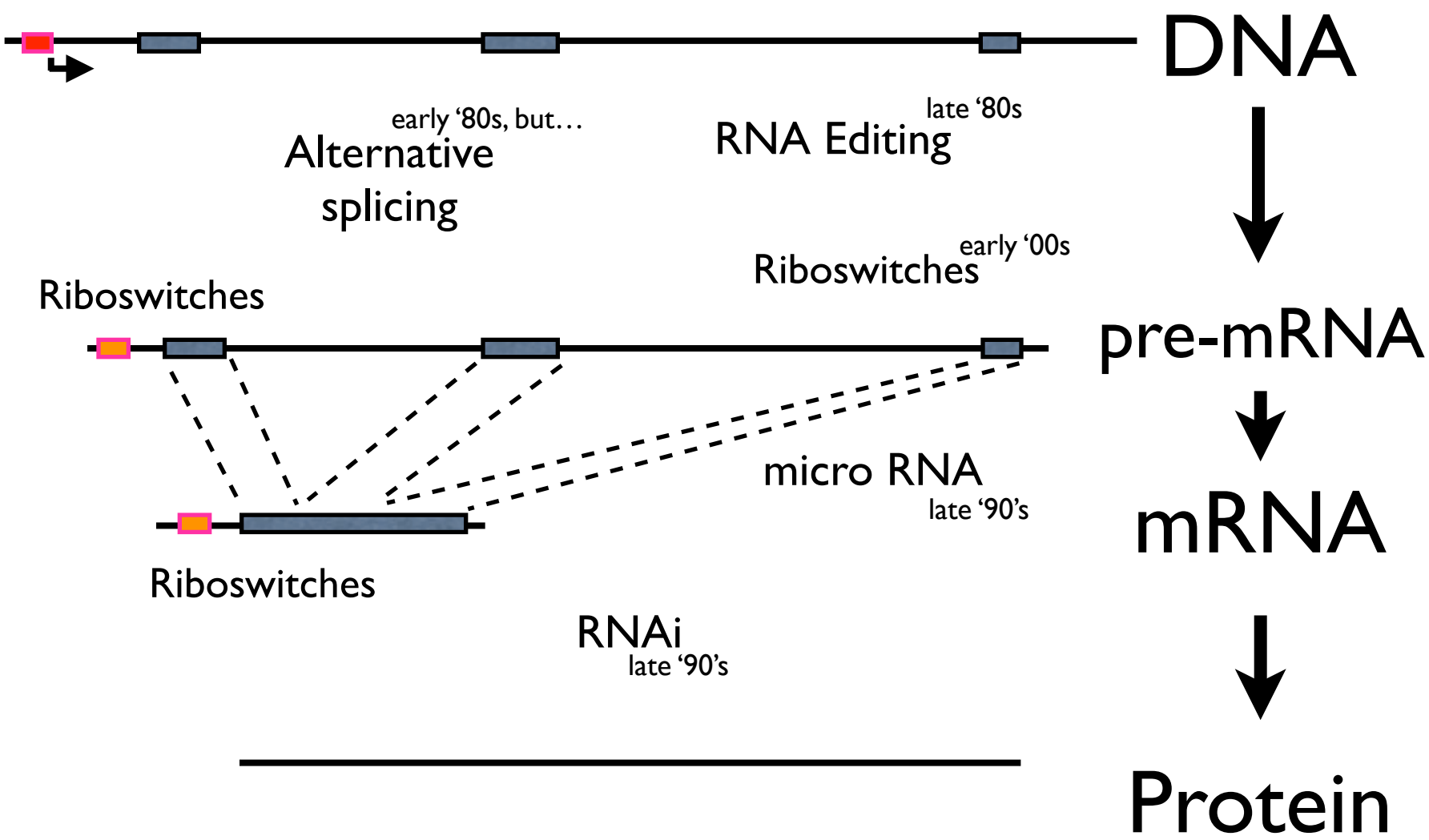

21st Century Opportunities