SELEXzyme

Evolving DNAzymes for Target Sequences

02-601 Project Presentation

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December 2, 2020

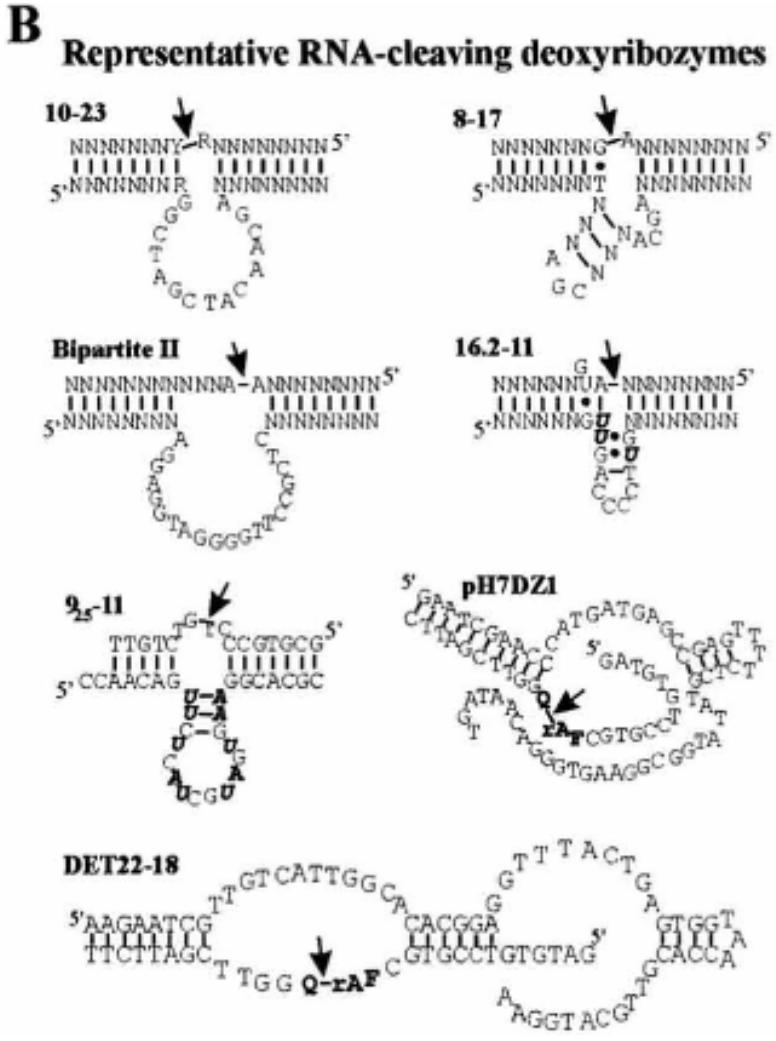
Summary

1. DNAzymes
2. SELEX and Genetic Algorithms
3. SELEXzyme

What is a DNAzyme?

Achenbach et al., 2004

What is a DNAzyme?



- Short DNA sequences with catalytic activity

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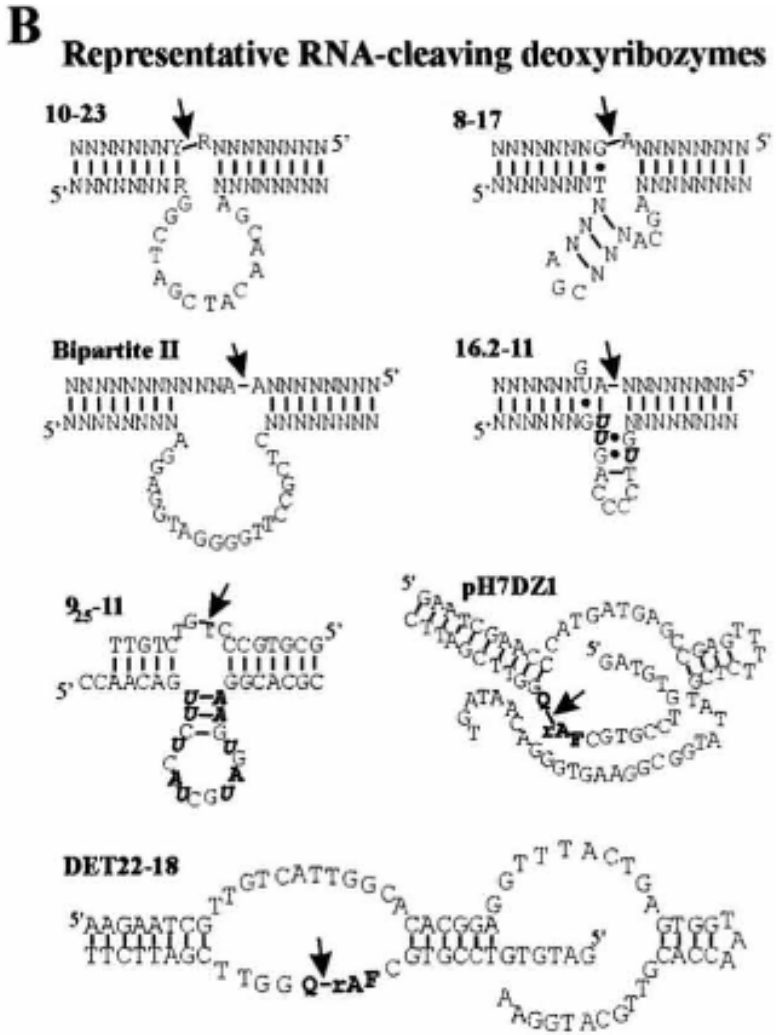

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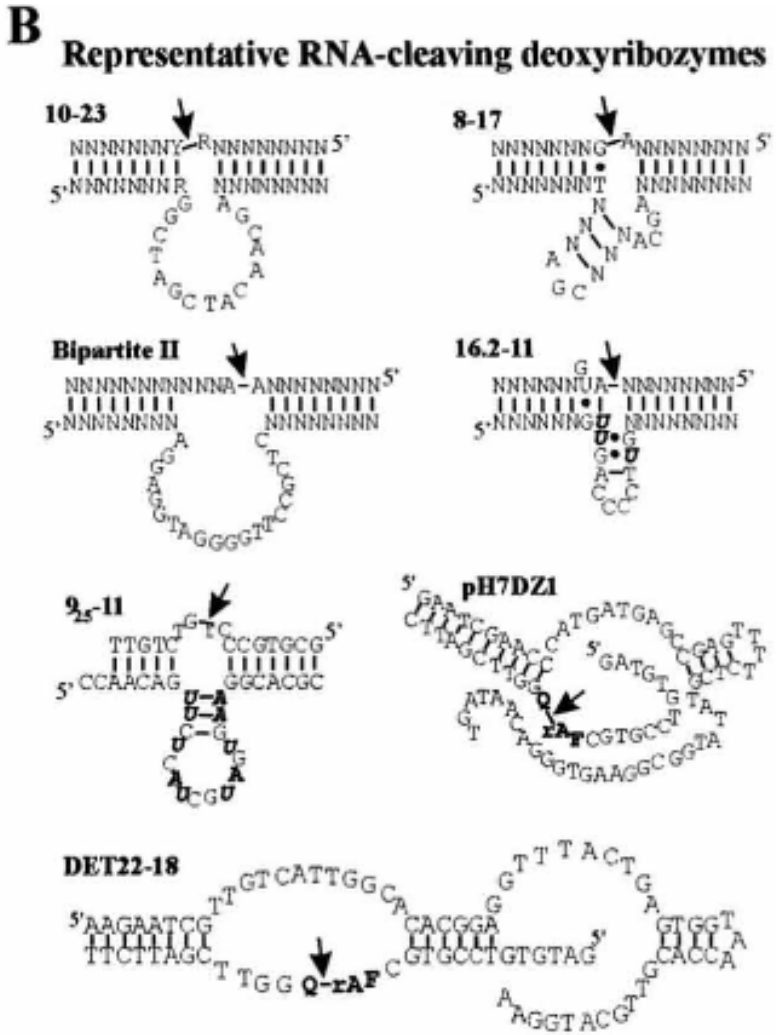

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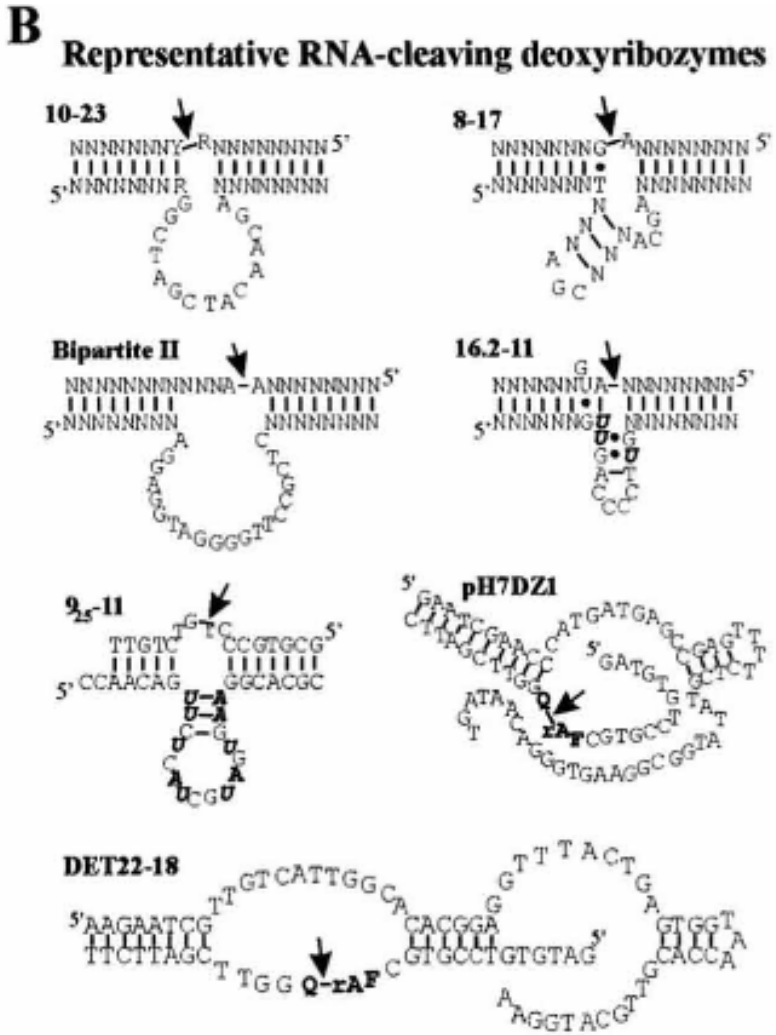

- Short DNA sequences with catalytic activity
- Often cut target nucleotide sequences
- Can have tertiary structure
- Never before observed *in vivo*

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Why Care About DNAzymes?

Lu and Liu, 2006;Morrison, Rothenbroker, and Li, 2018

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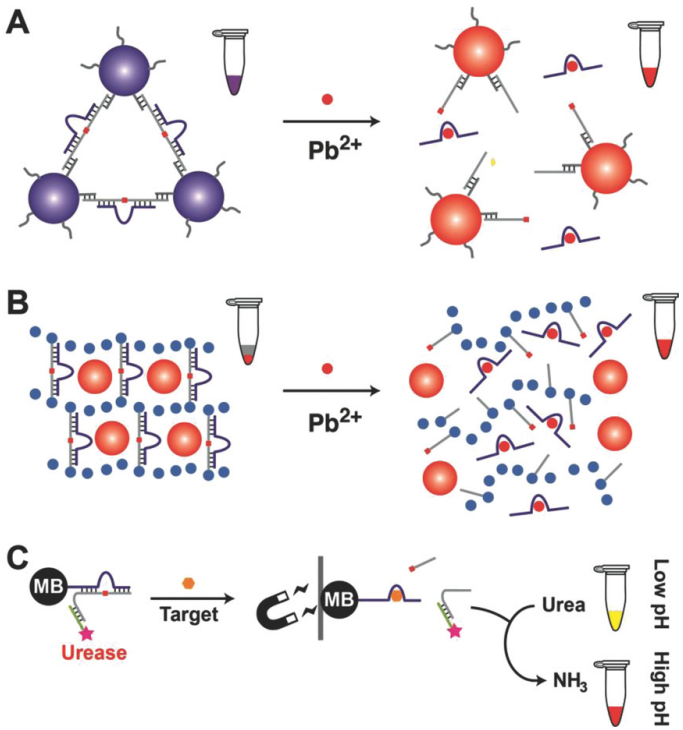

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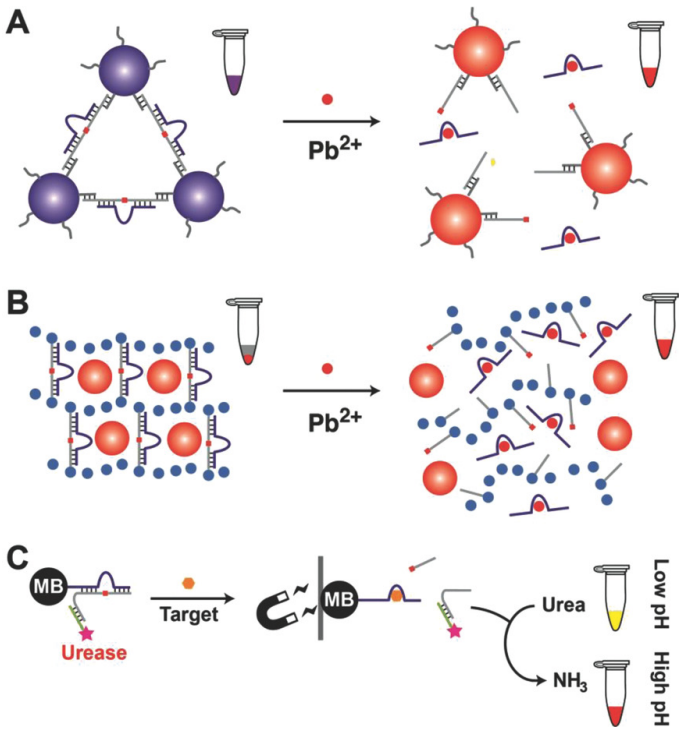

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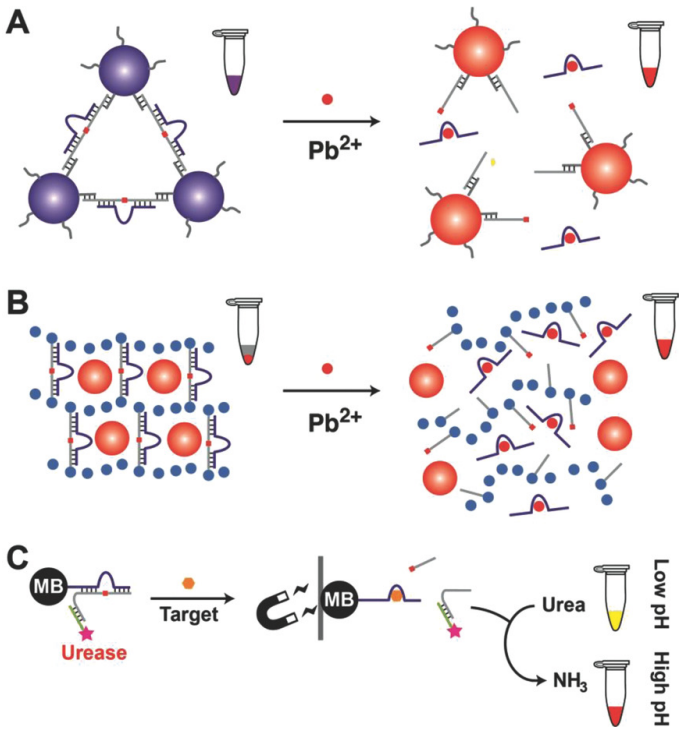

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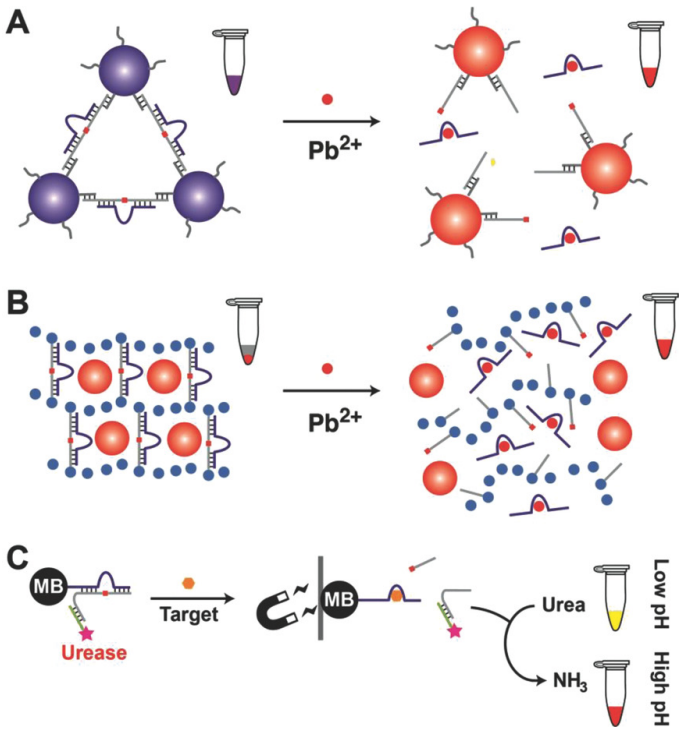

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- Can encode logic into DNAzyme constructs
- Often combined with DNA Aptamers i.e. DNA antibodies

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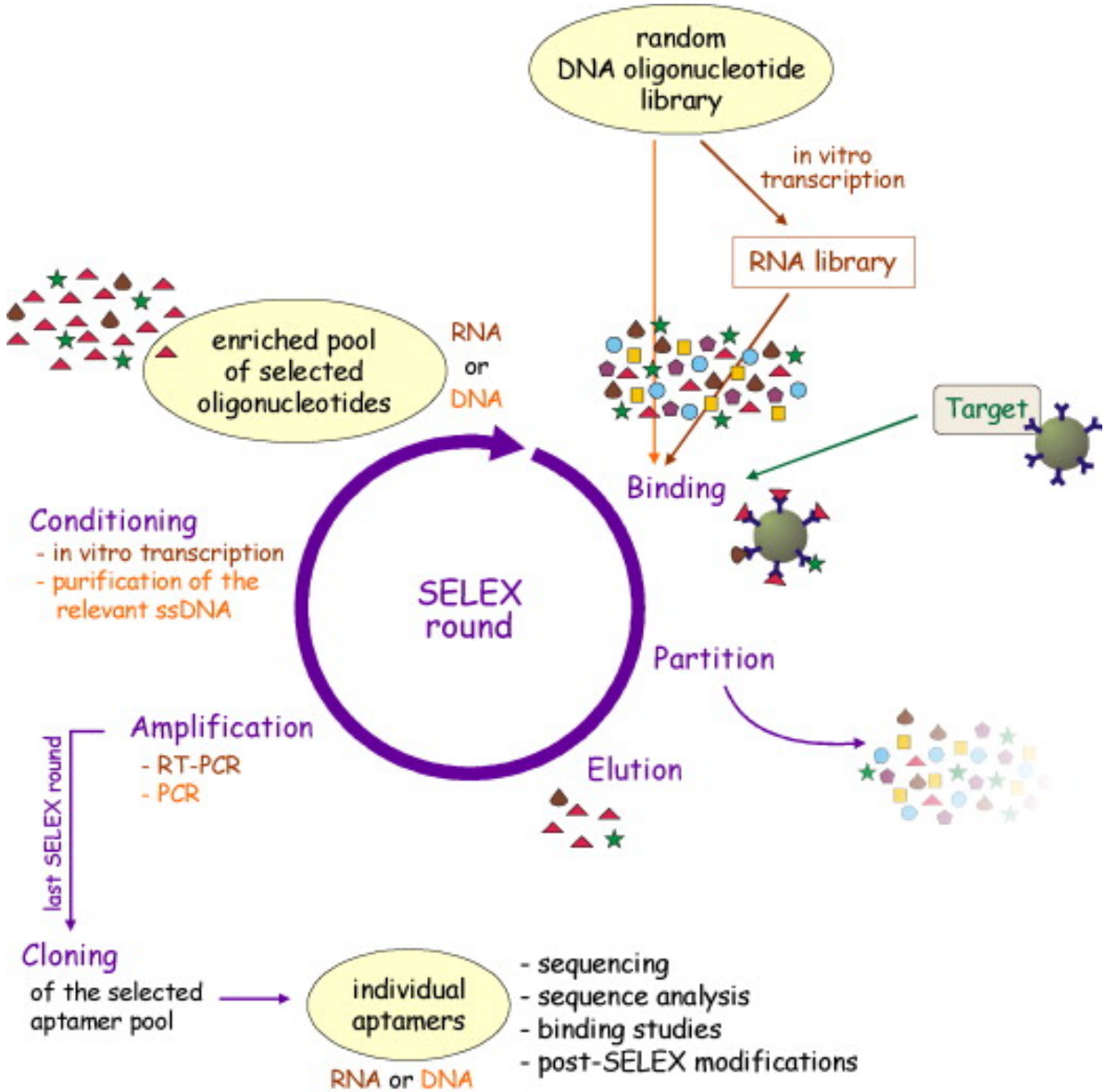
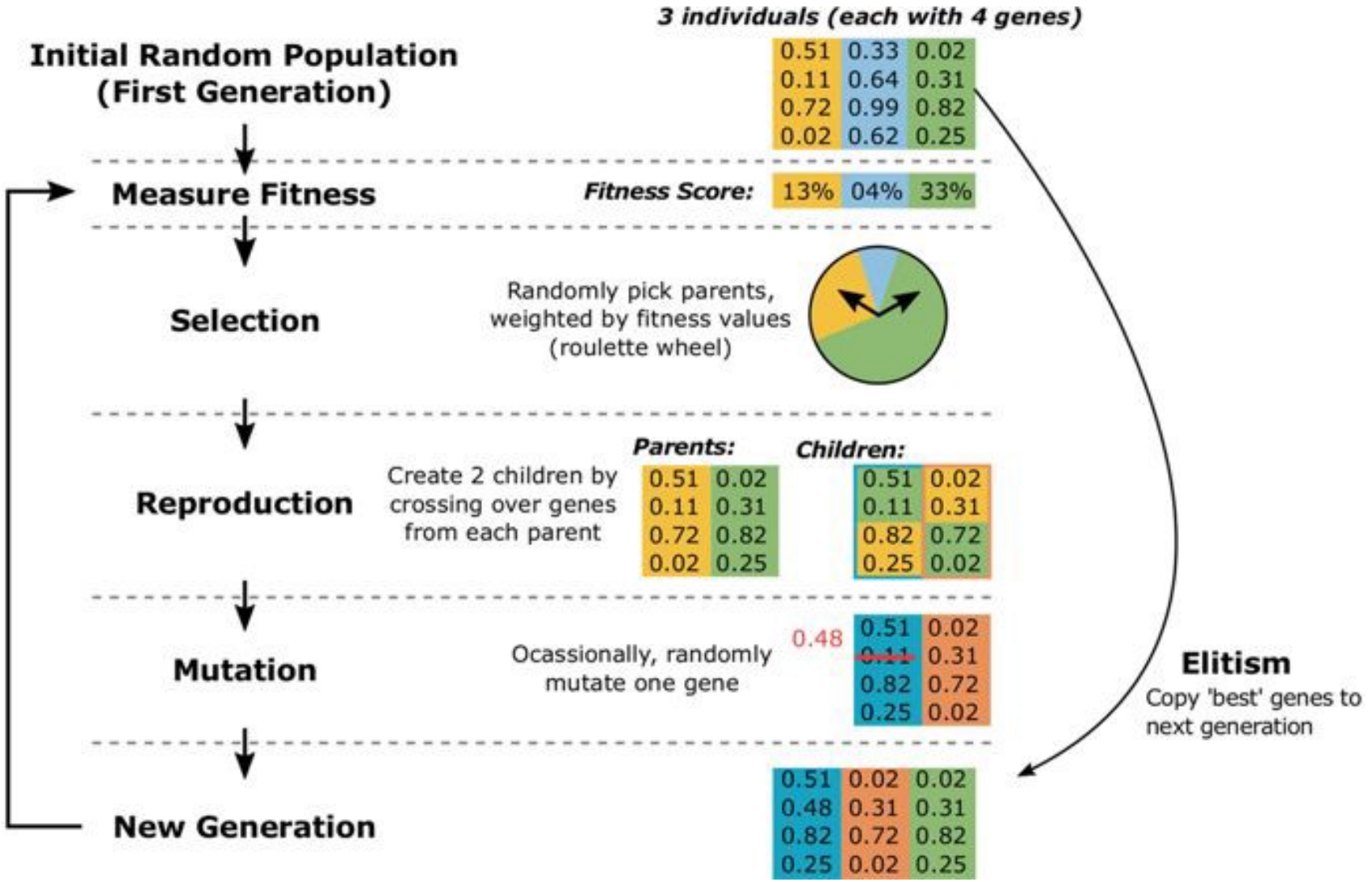
How Do You Design DNAzymes?



Stoltenburg, Reinemann, and Strehlitz, 2007

Genetic Algorithms Simulate SELEX



Bal, 2019

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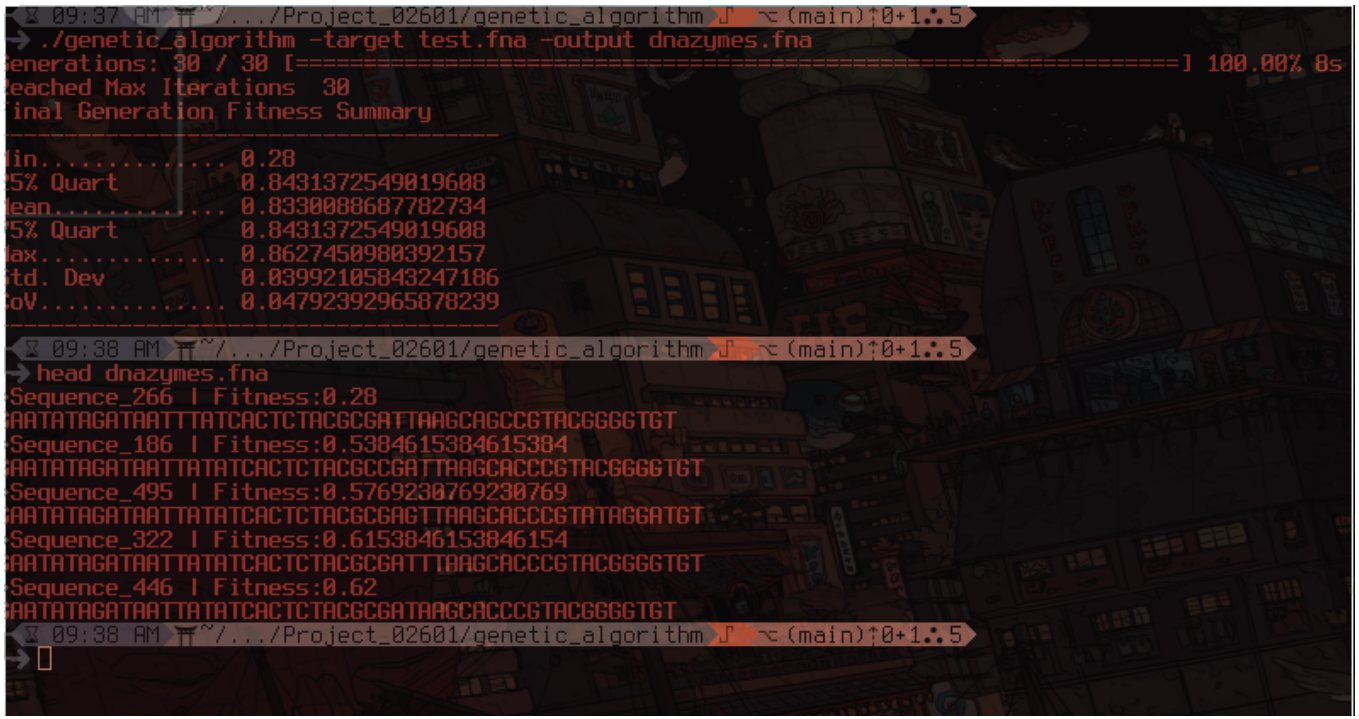

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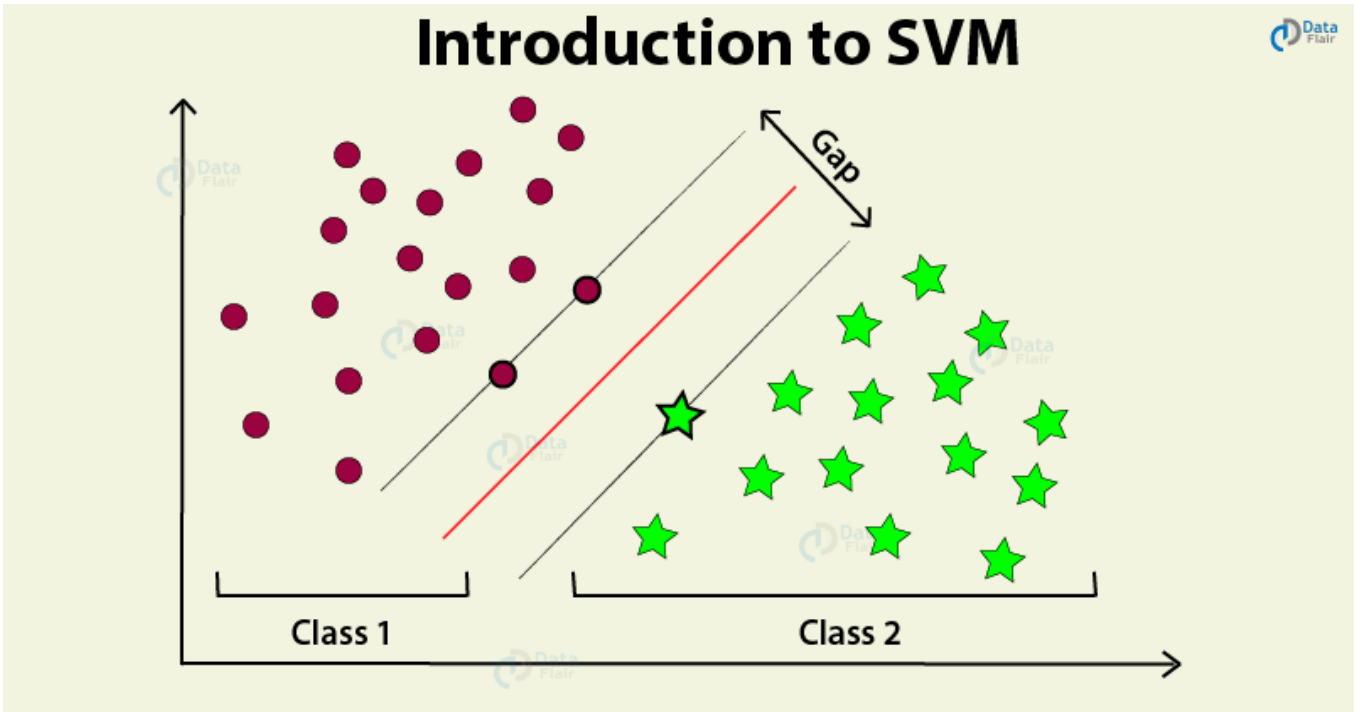
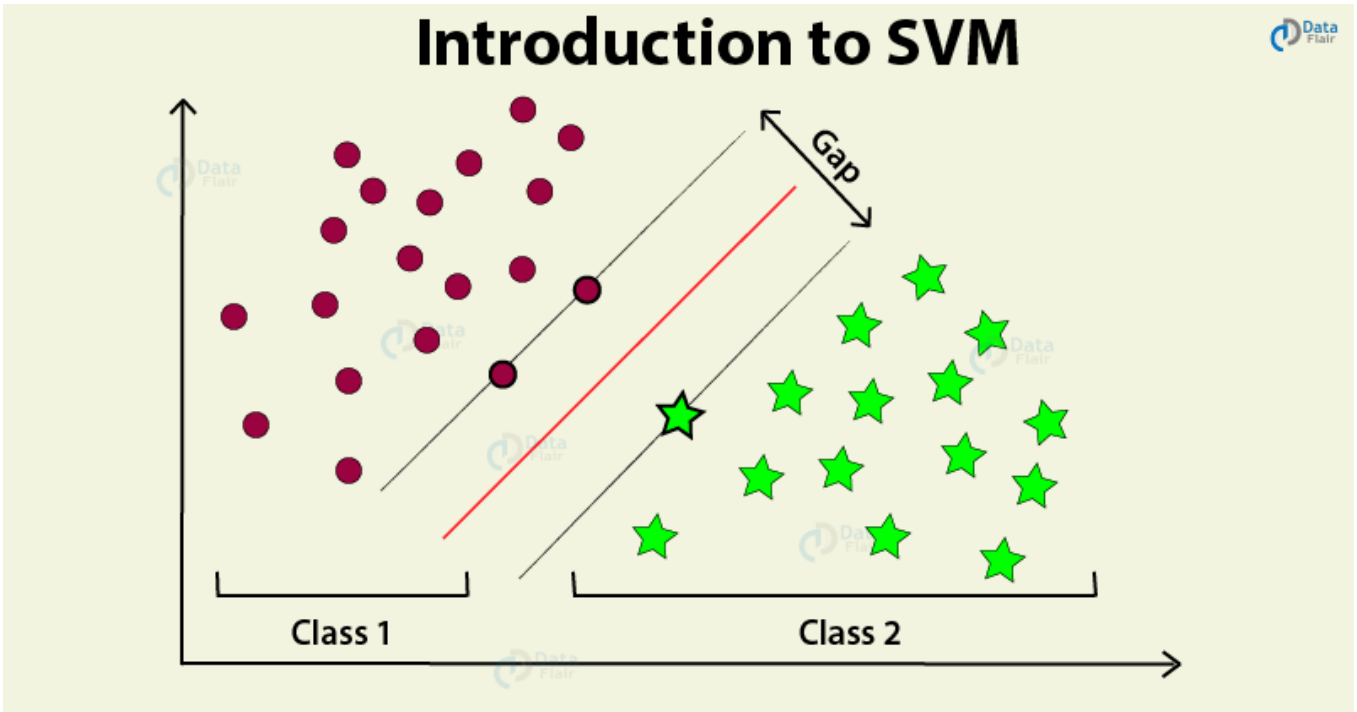


Xing, Pei, and Keogh, 2010;Flair, 2017

What is the Fitness Function?

- Smith-Waterman alignment score to user target sequence
- Probability of being a DNAzyme from the ML model
- Use an SVM model, good for simplicity vs quality trade-off
- Model trained on known DNAzymes, DNA aptamers, Promoters and simulated data



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Validation

J RNAi Gene Silencing. 2005 Oct; 1(2): 88–96.
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Design of efficient DNAzymes against muscle AChR α-subunit cRNA *in vitro* and in HEK 293 cells

Amr Abdelgany,[1] M Khabir Uddin,[2,3] Matthew Wood,[4] Kazunari Taira,[2,5] and David Beeson[1,*]

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- Similar sequence composition (high alignment score)
- *in vitro* screened DNAzymes should have high fitness values

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