In Silico Tertiary-Structure-Based RNA Aptamer Design

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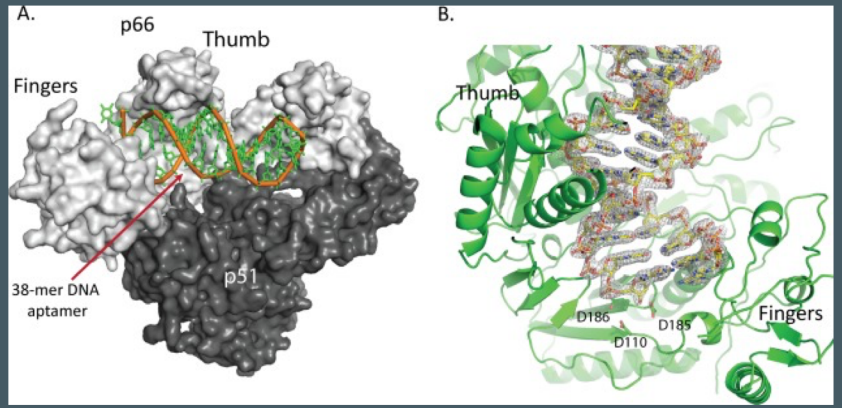
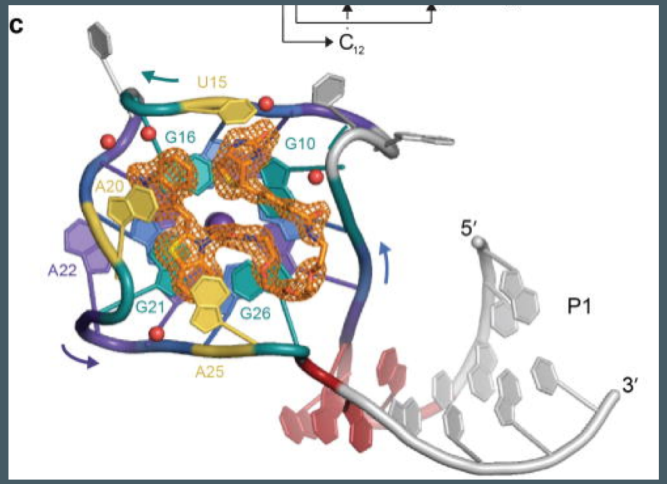
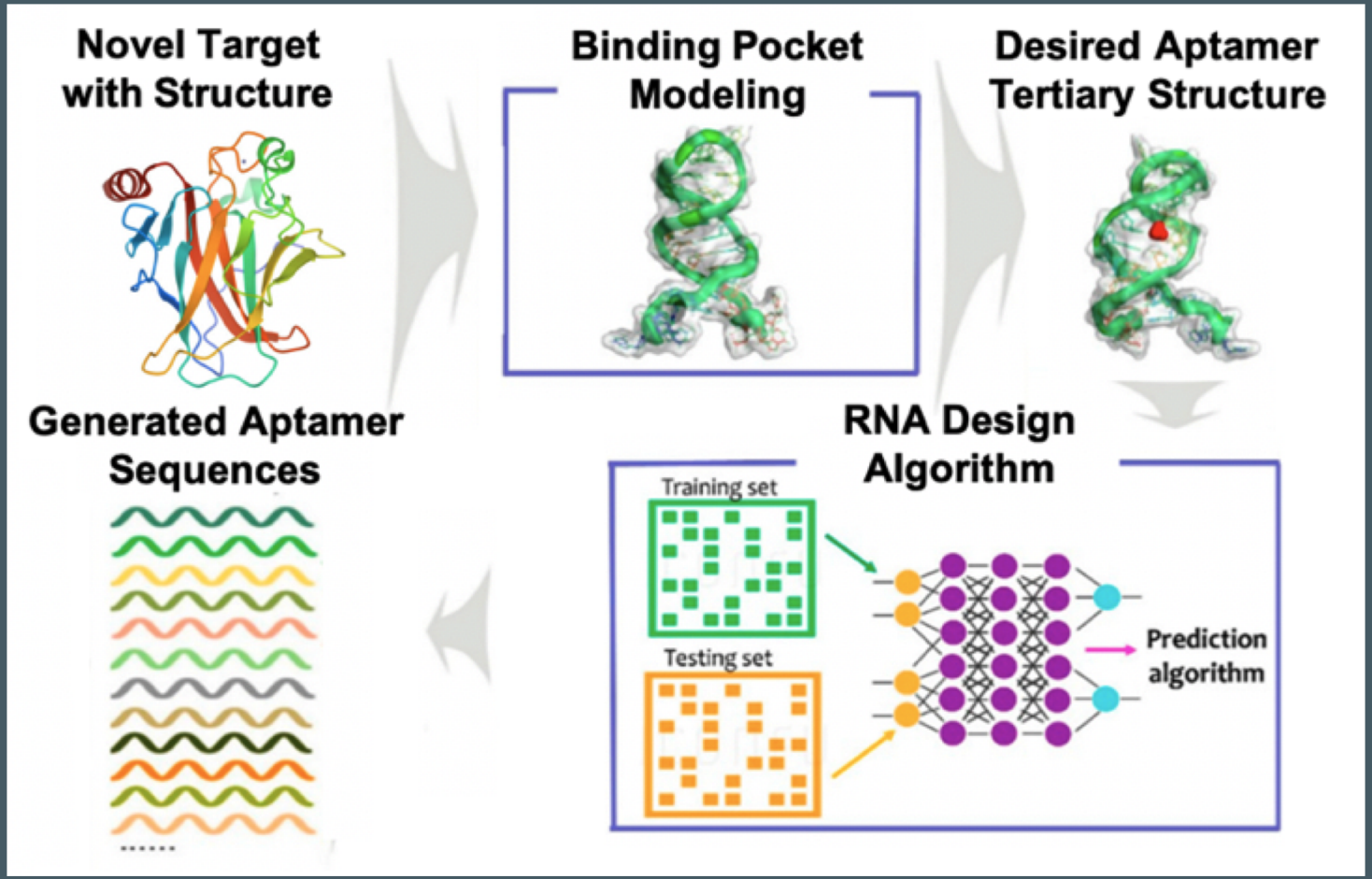
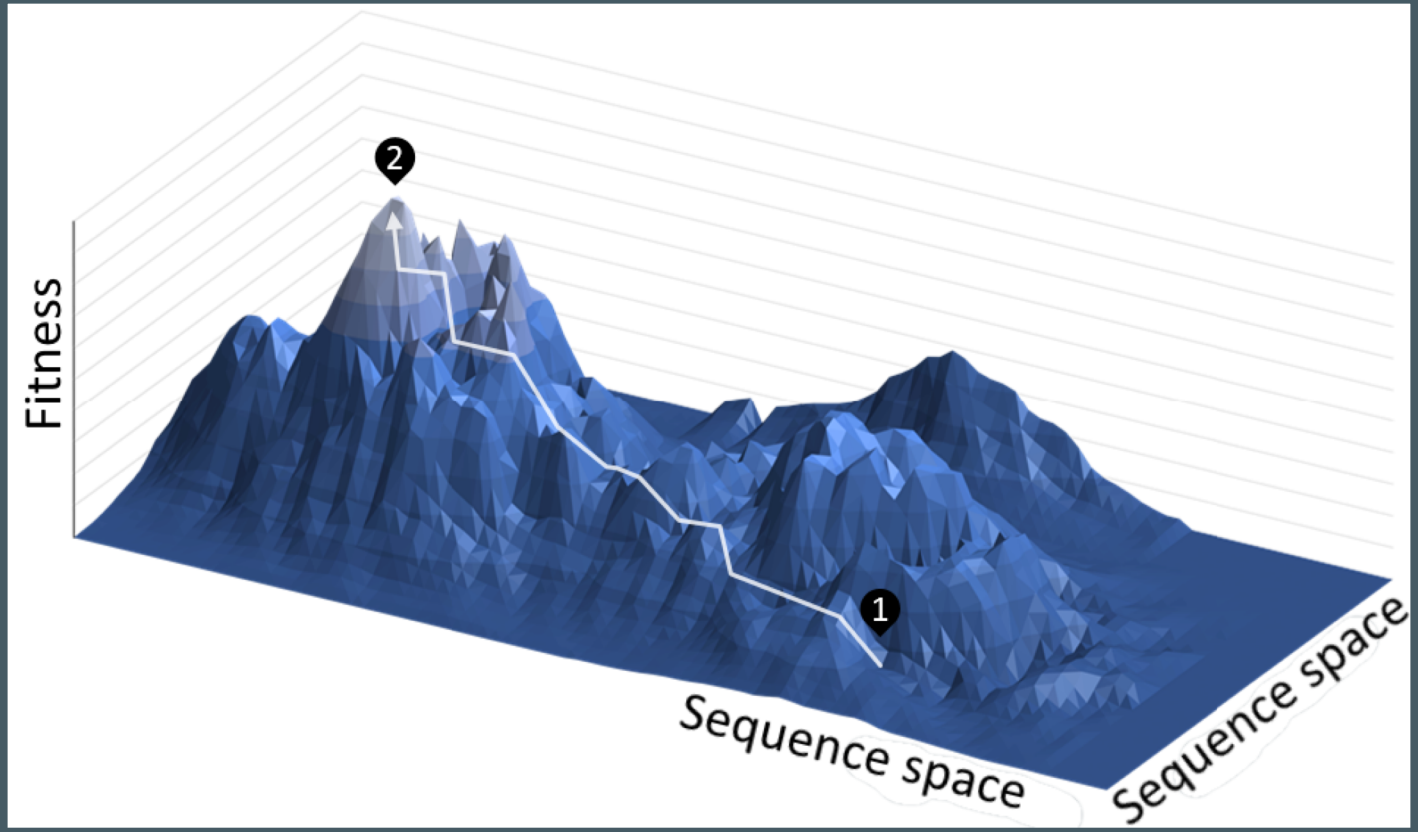
RNA Aptamers

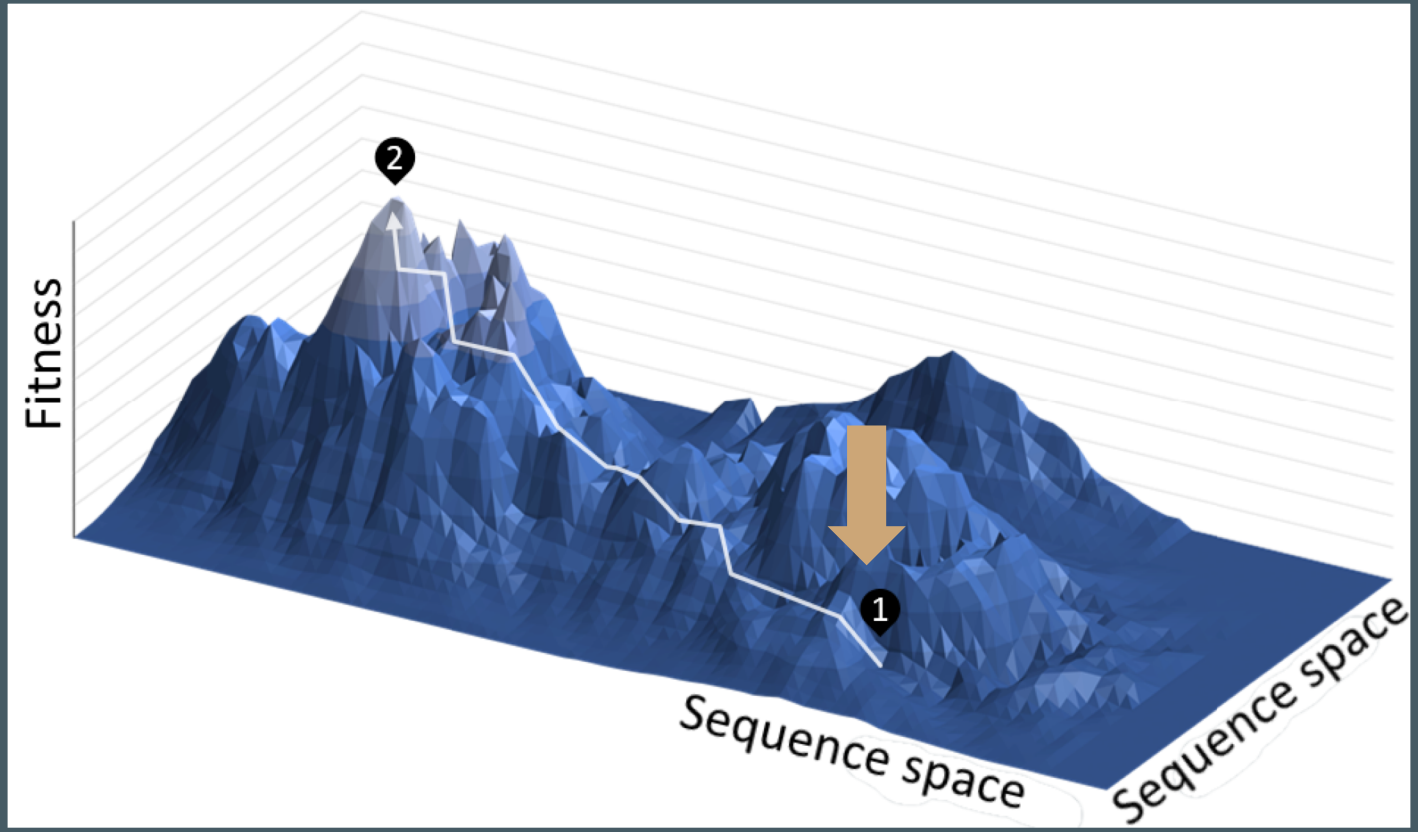
- **Selective and Sensitive Binding**
- Easier chemical synthesis
- Small size
  - Tissue penetrance






Novel Target with Structure
Binding Pocket Modeling
Desired Aptamer Tertiary Structure
Generated Aptamer Sequences
RNA Design Algorithm
Training set
Testing set
Prediction algorithm


Fitness
2
1
Sequence space
Sequence space


Fitness
2
1
Sequence space
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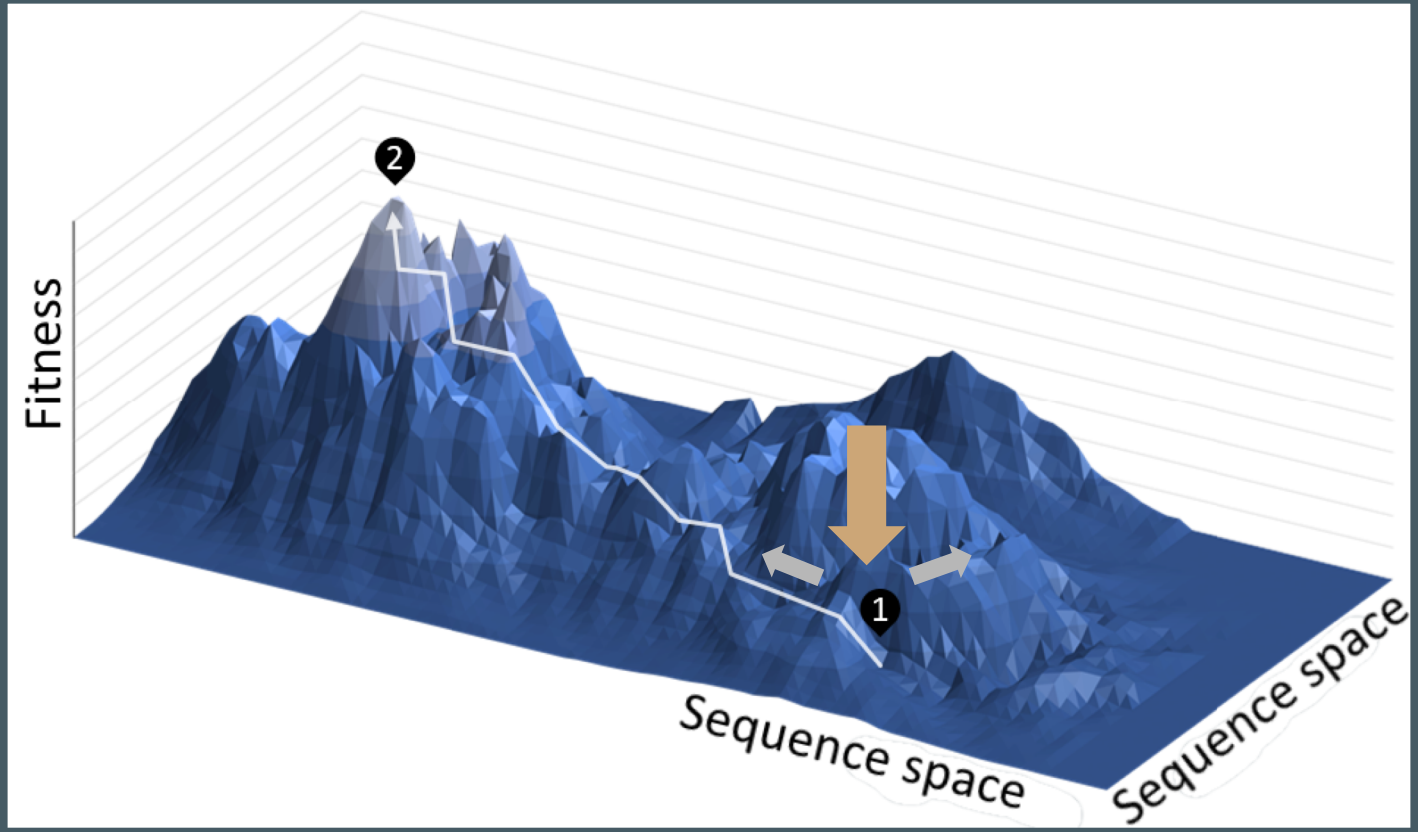
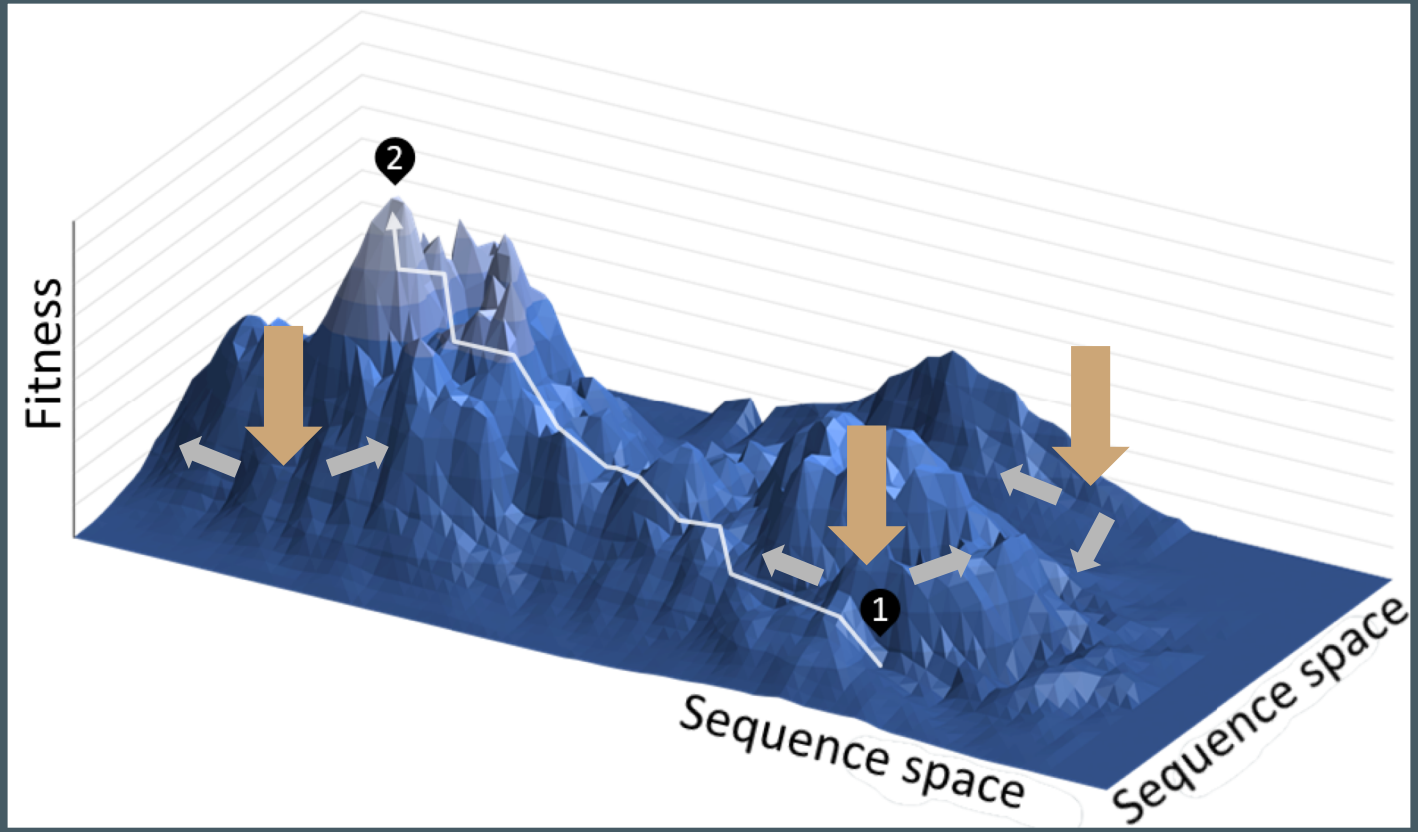

Fitness
2
1
Sequence space
Sequence space


Fitness
2
1
Sequence space
Sequence space

Preliminary Performance

16 threads ⇒ ≈ 2-4x speedup

Scientific ML to Augment Experimental Validation

- Training Data: First round of experimental candidate validation
- Biophysics-informed NN to model aptamer-target binding (expensive to determine experimentally)
- Input: 4 (number of nucleotides – A, U, C, G) x n (length of desired aptamer)
- Output: Binding Affinity
- NN Interpretation: Network weights indicate importance of specific positions and domains on molecule

Citations

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