Learning the RNA inverse folding problem.

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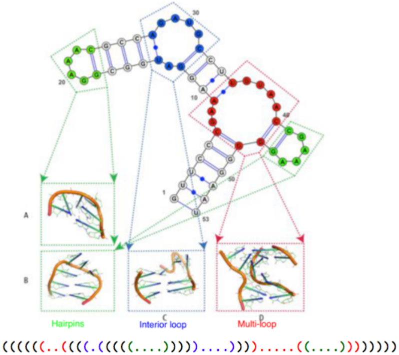
Structure Prediction a.k.a. Folding



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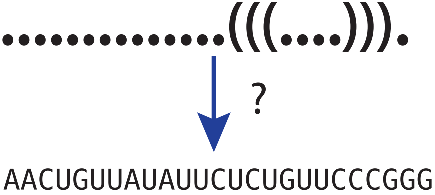
- Input: RNA sequence $x_1, x_2, ..., x_N$ where $x_i \in \{A, U, C, G\}$
- Output: RNA 2D structure $\omega = \{(i, j), ...\}$ where i and j are indices in the sequence x that are paired.
- Solution: Dynamic Programming + physics based rules.
- Current approaches achieve high accuracy in $\mathcal{O}(n^3)$ time for sequences of length < 200.

Structure Design a.k.a. Inverse Folding



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- Input: 2D Structure
- Output: sequence whose minimum energy fold corresponds to the input.
- Key problem for synthetic biology and drug design.
- Current solutions: local search strategies
- No linear time algorithms exist to solve this problem.

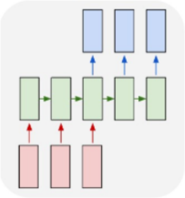
Data

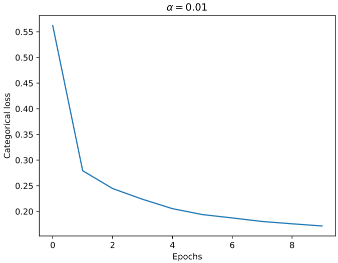
Two types of sequence-structure data:

- Real world
  - Rfam databse (hand curated sequences for structural families): $\mathcal{O}(100K - 1M)$ sequences per family
- Artificial
  - Local search software for design: unlimited data size

Approach: One model → one structure

- Generate sequences belonging to one of 5 Rfam structural families.
- Given set of member sequences, generate novel likely members.
- Model: RNN + LSTM
- Evaluation: Covariance models, GC content, base pair distance, discriminator NN.





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training: > --CUUGAC-GA-U-C-AU-AGA----GC-G-U-U-G---GA----------A-CC-A--------
RNN:      > GAUG----GUACUGCG---UCU--CAA-G-ACGUG-GGA---G---AGUA----GG-U-CA-CC-
          > UCU--CAA-G-ACGUG-GGA---G---AGUA----GG-U-CA-CC--G-CCGGUC--GUGG----
          > AUU---ACCUGUA----------AAA-----AGUUG---GA-----GGG-----AAC------CC
          > --GGCCCUA-G-UUC--AU-CCAAG----AGUU-------A-----GUUA---AAUCCCC-----
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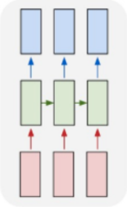
Approach: One model → all structures



- Goal: generate a likely sequence for a given structure.
- Input: vector representations $s_i \in \{0,1\}^{|\omega|}$ for each index i in structure ω where

$$s_i[j] = \begin{cases} 1 & i \text{ paired with } j \\ 0 & \text{else} \end{cases}$$

  - Output: 1 of 4 encoding of the nucleotide in $\{A, U, C, G\}$ belonging to position i in structure.
  - Approach: sequence to sequence RNN, LSTM. Recursive NN.
  - Long term goal