# Introduction: Structure Prediction/Design for Nucleic Acids and Complexes

CS/CME/Biophys/BMI 371

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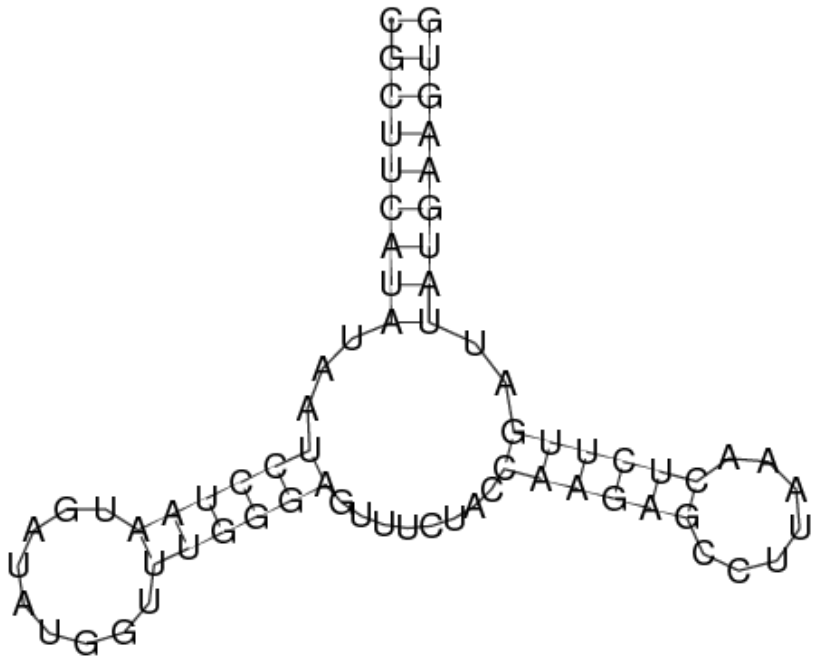
# Nucleic acid structure

- Most of the “machines” in the cell are protein-based
- Nucleic acids (DNA and RNA) act primarily as information carriers
- However, they’re not just long threads. They can take on well-defined structure, which is important in two ways:
  - It influences gene expression (the extent to which proteins are produced from the DNA that codes for them)
  - Nucleic acids—especially RNAs—can also act as machines. (Maybe life originated this way.)

# Topic 1: Predicting RNA secondary structure

- For RNA “secondary structure” — that is, how the bases pair — is of great interest

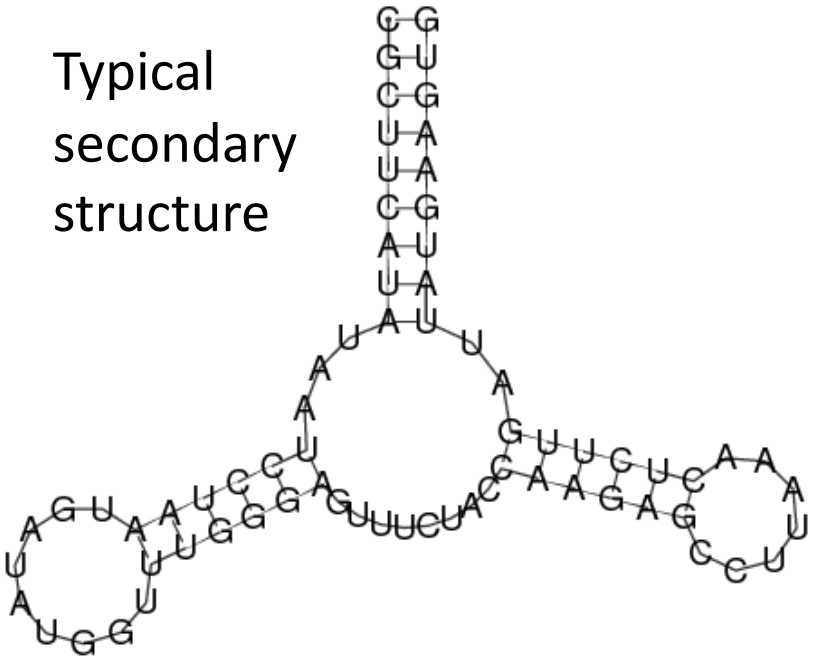


http://www.tbi.univie.ac.at/~pkerp/forgi/_images/1y26_ss.png

# Predicting secondary structure of RNA pseudo knots

- RNA secondary structure is typically predicted using dynamic programming algorithms that assume all loops are “nested”
- *Pseudoknots* violate this assumption
- One of Thursday’s paper proposes an algorithm to overcome this problem, incorporating information from SHAPE experiments (also used in EteRNA)

Typical secondary structure



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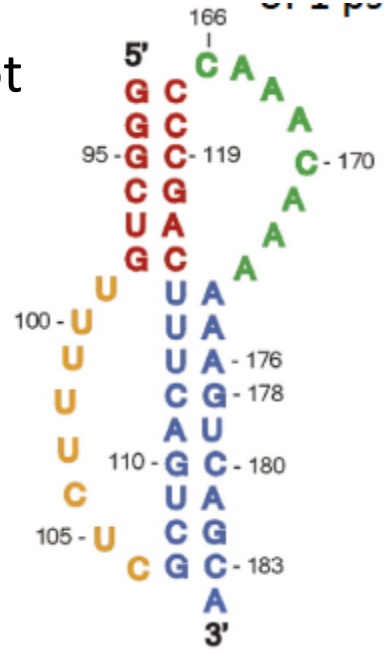
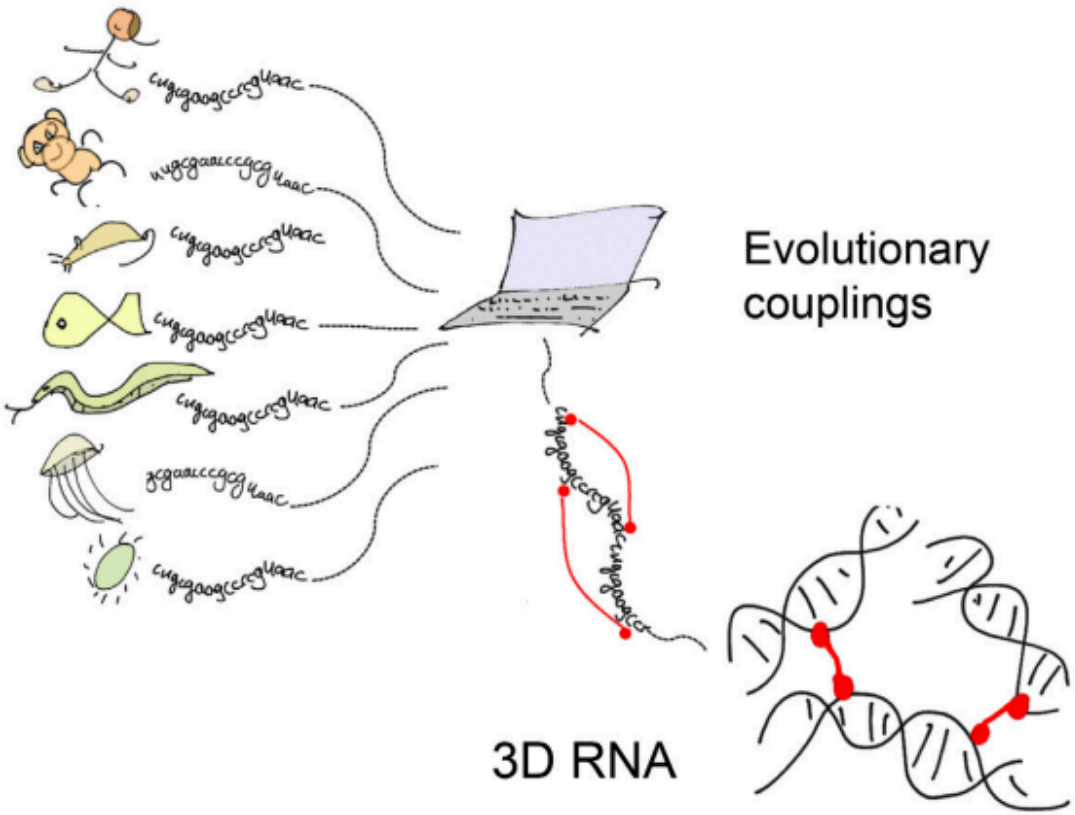
Pseudoknot




Theimer and Feigon, Curr. Opin. Struct. Biol. 16:307-318 (2006)

# Topic 2: Predicting RNA 3D structure by evolutionary coupling analysis

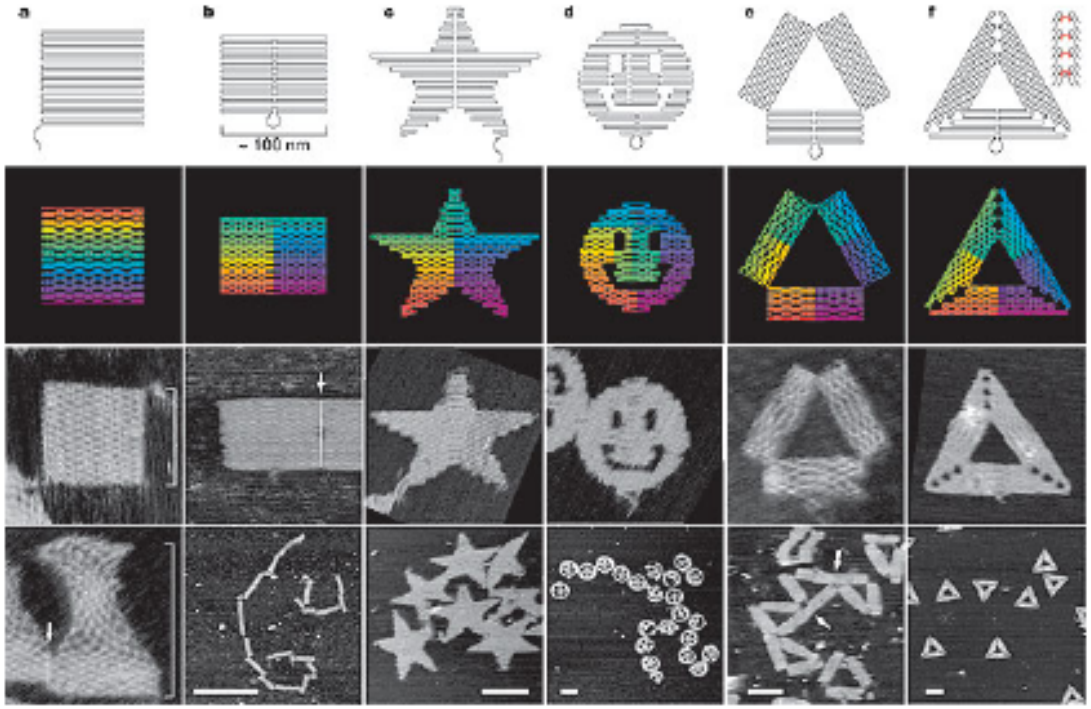
- The “coevolution” idea works not only for proteins but also for RNAs:
  - Given sequences of many related RNAs, one can identify pairs of bases that coevolve because they are in physical contact
  - This information helps predict 3D structure

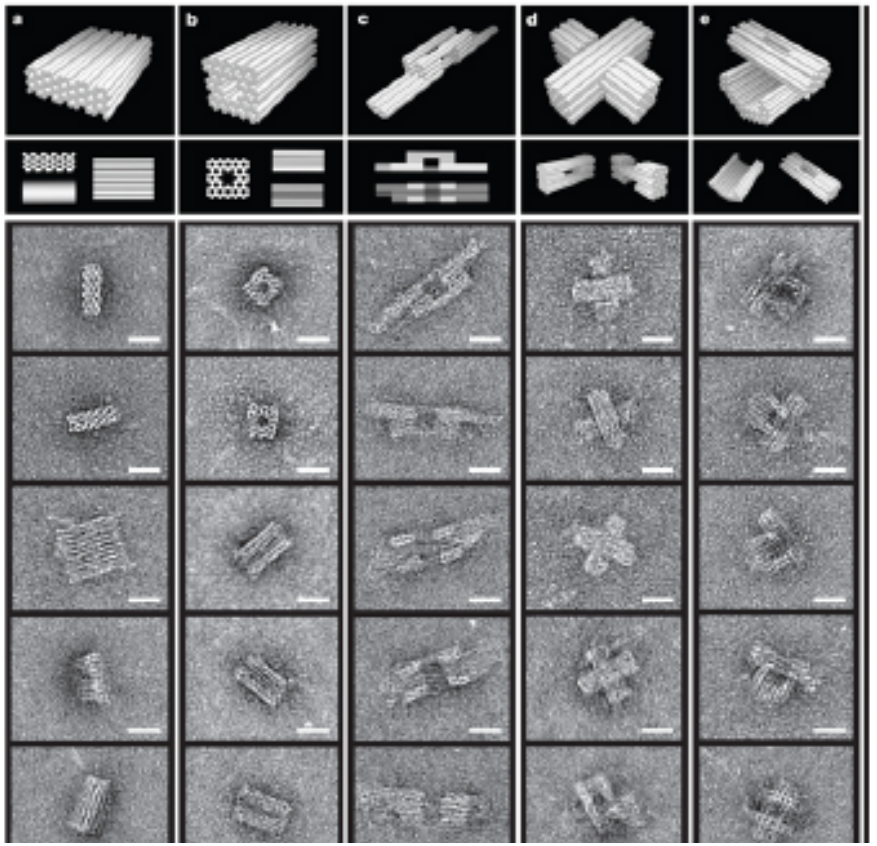



Weinreb et al., Cell 165:963-75, 2016

# Topic 3: Design of DNA structures

- DNA has been used previously to design "origami" shapes

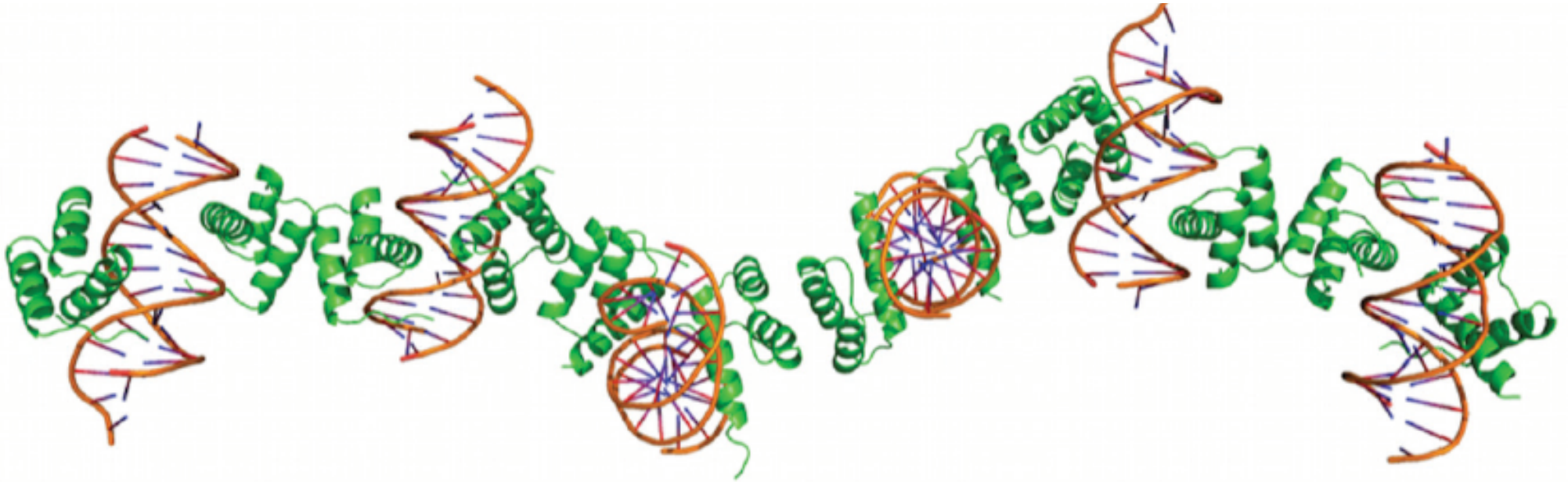



PWK Rothemund. Nature 440, 272-302 (2006).
SM Douglas et al. Nature 459, 414-418 (2009).

# Designing a DNA–protein complex

- One of Thursday's papers describes design of a self-assembling "wire" including repeating protein and DNA units



Mou et al., Nature 525:230-233 (2015)