RNA Structures

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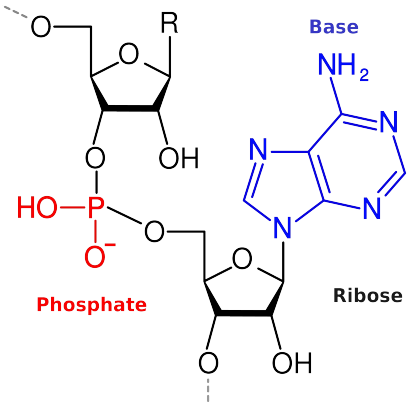
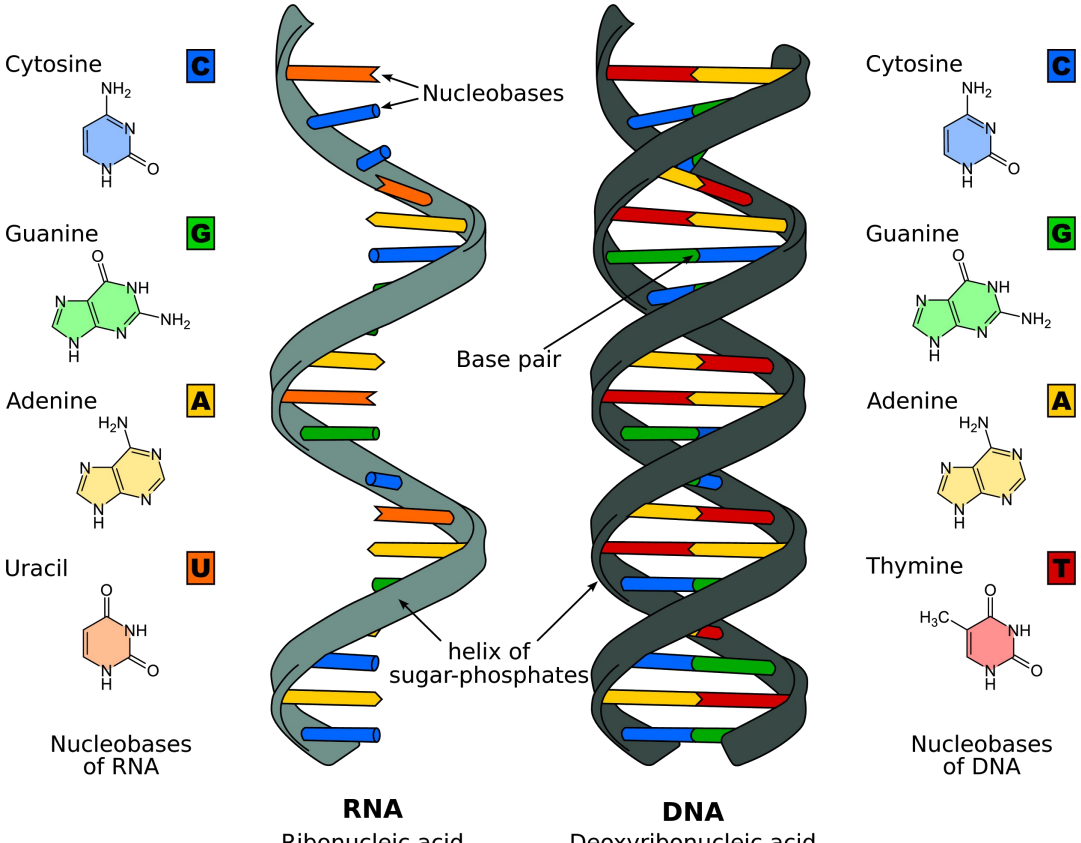
Plan

- Intro
  - What is RNA?
  - Why is it important?
- Structure
  - Important interactions
  - Common structural motifs
- Experimental structure resolution
  - X-ray, NMR
  - FRET, etc…
- Computational tools
  - Molecular dynamics
  - Hands-on structure visualisation

RNA and DNA

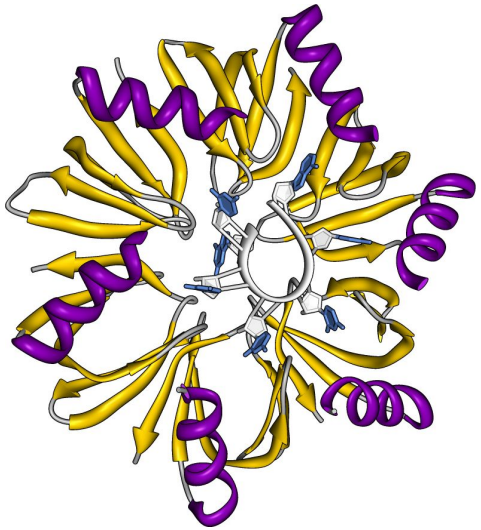
- Polymer
- Highly charged
- 4 common bases
- Takes various shapes

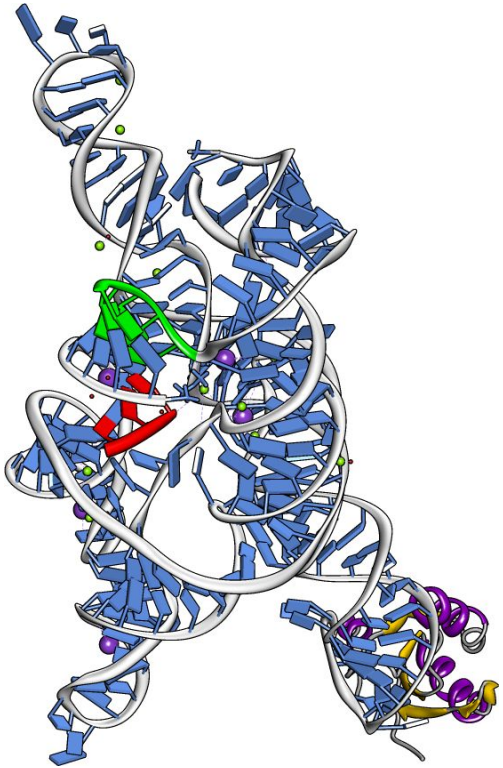




Roles of RNA

- Catalysis
- Signaling
- Gene regulation

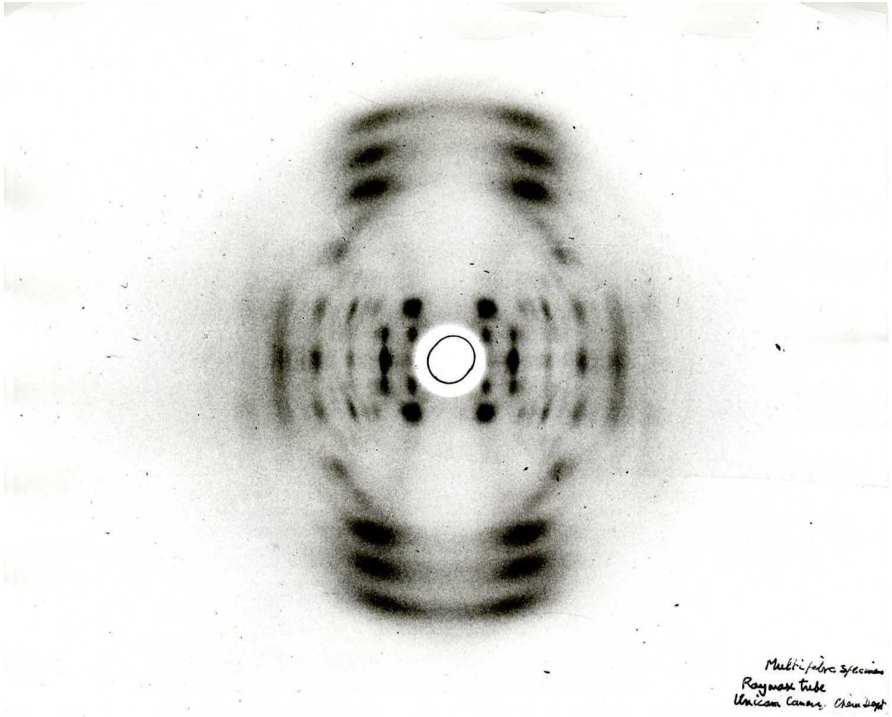




Experimental structure resolution

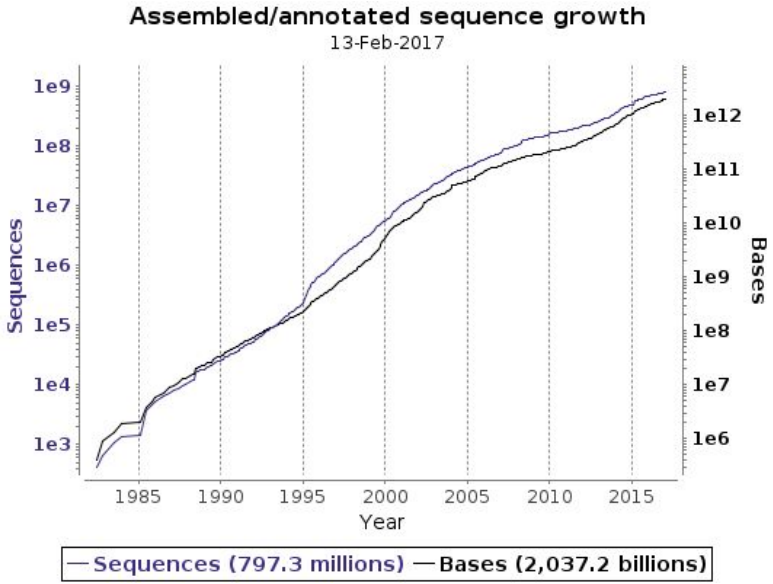
X-ray crystallography

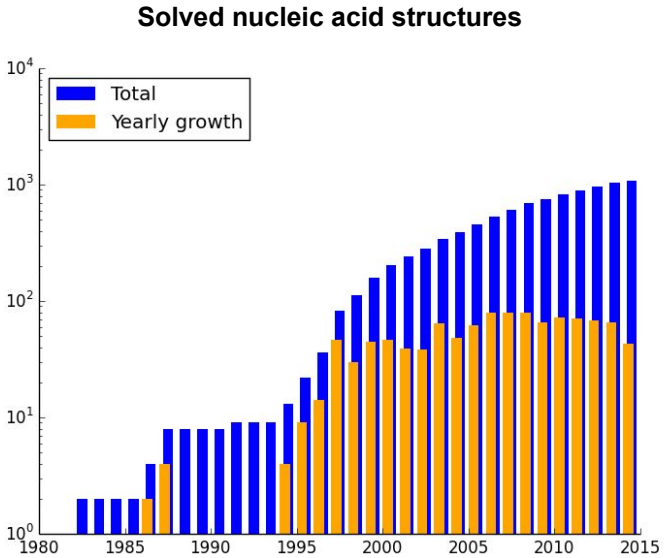
- First method that provided nucleic acid structure (Rosalind Franklin, Watson and Crick)
- X-ray beam produces a diffraction pattern when shone on an object (usually a crystal)
- The diffraction pattern contains information about the structure



X-ray crystallography

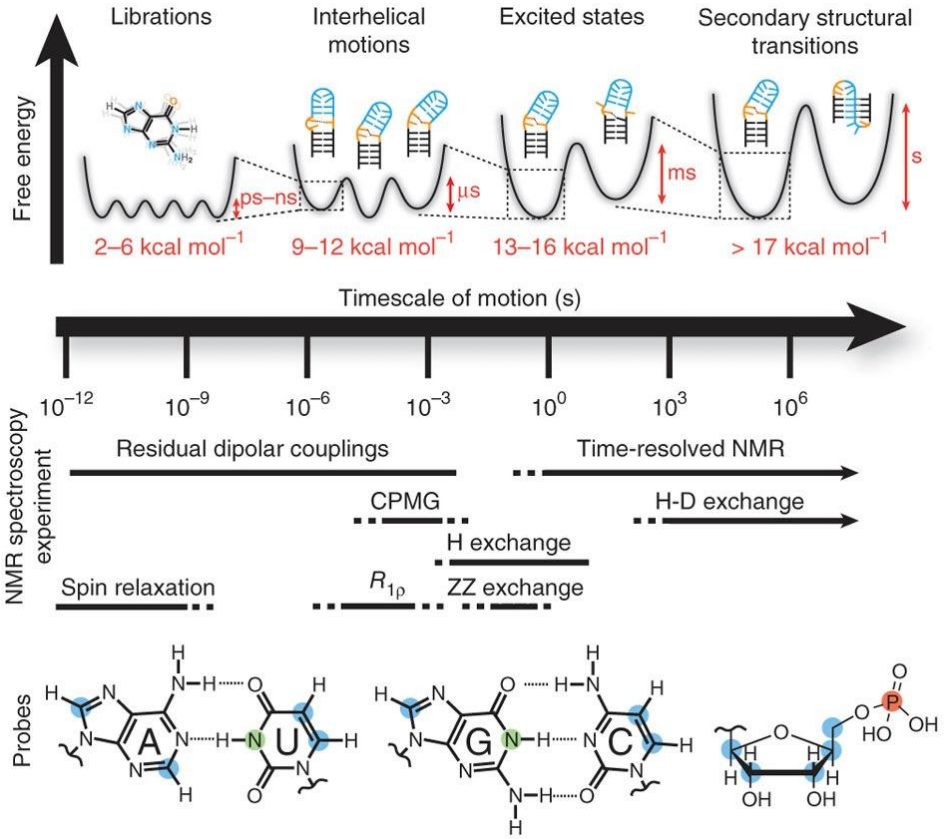
- Creating crystals of large molecule is difficult, and costly
- Gap between solved structures and sequences is increasing





NMR

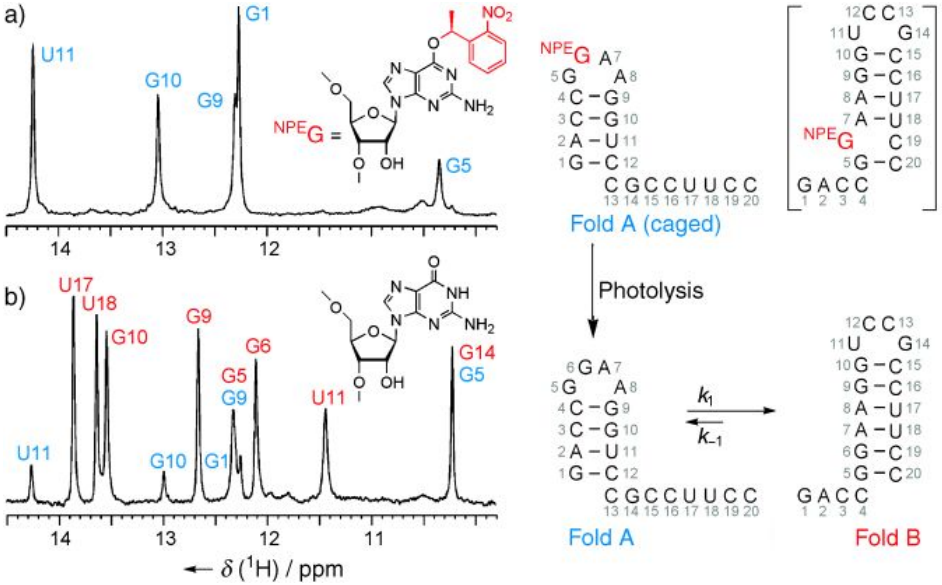
- Different techniques provide different structural informations
- Timescales involved range from picoseconds to hours



Bothe et al., Nature Methods 8.11 (Oct. 2011), pp. 919–931
doi: 10.1038/nmeth.1735

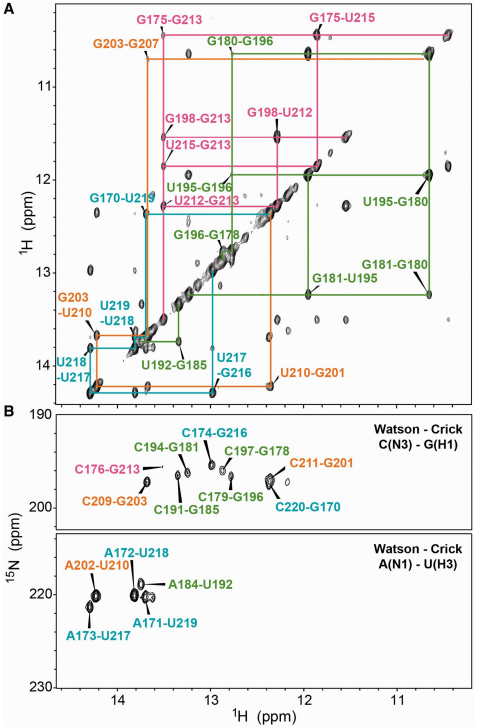
NMR

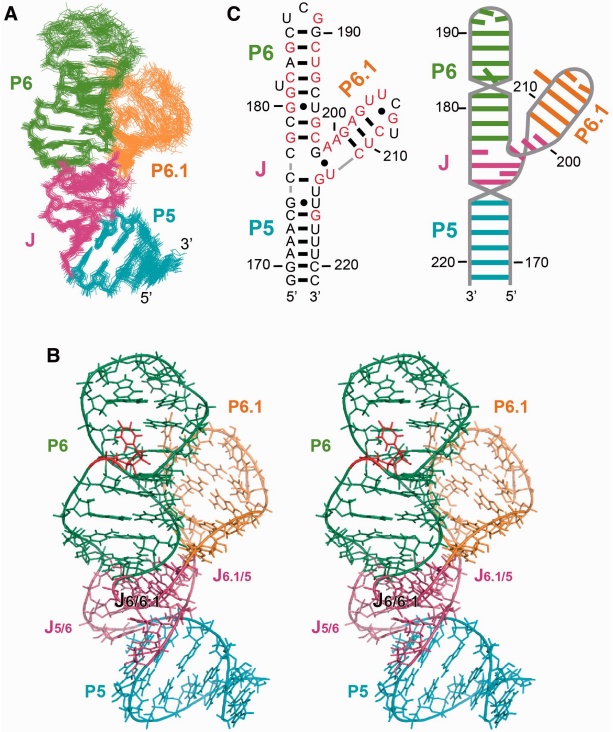
- The entire structure need to then be reconstructed from the data



Wenter et al., Angew. Chemie vol 44, no. 17, (Apr. 2005), pp. 2600-2603
doi: 10.1002/anie.200462724

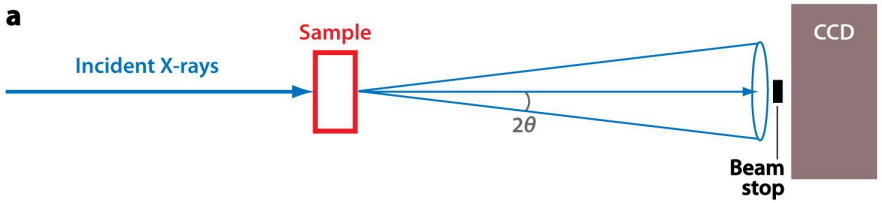
NMR

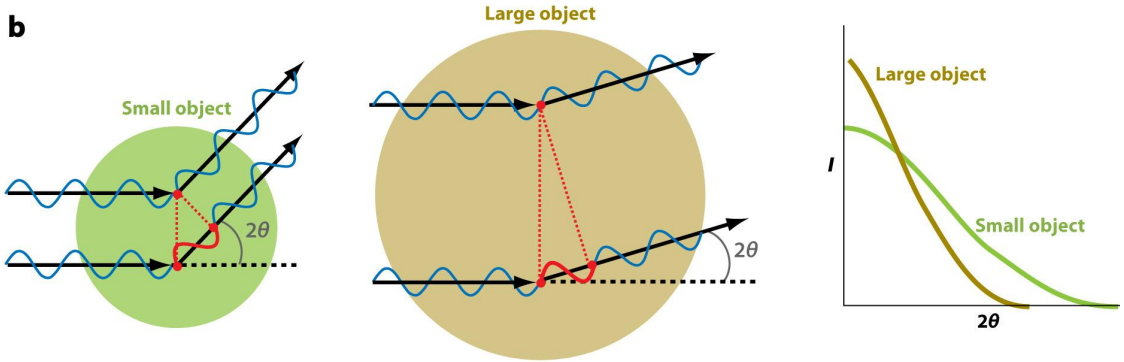


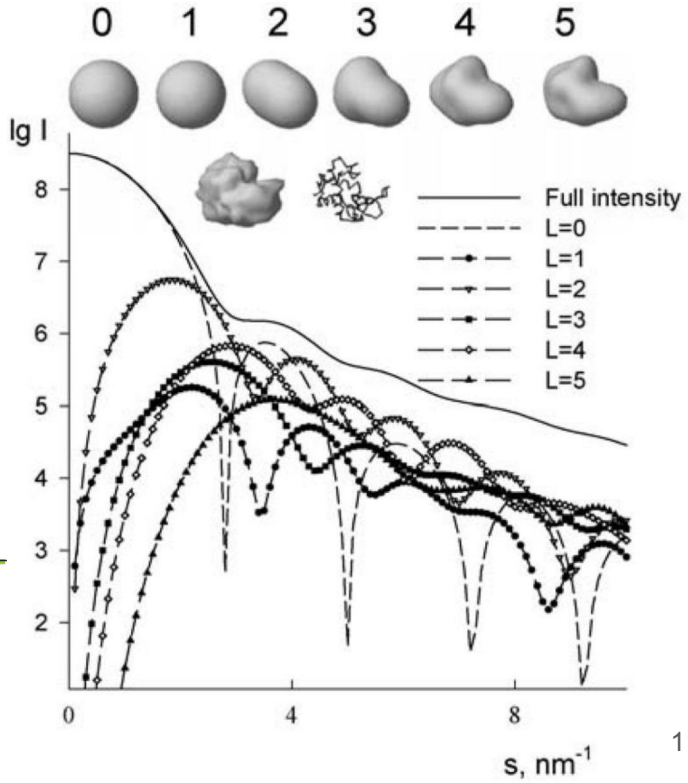


Kim et al., Nucleic Acids Res., vol. 42, no. 5, pp. 3395–408, Mar. 2014.
doi: 10.1093/nar/gkt1276

SAXS



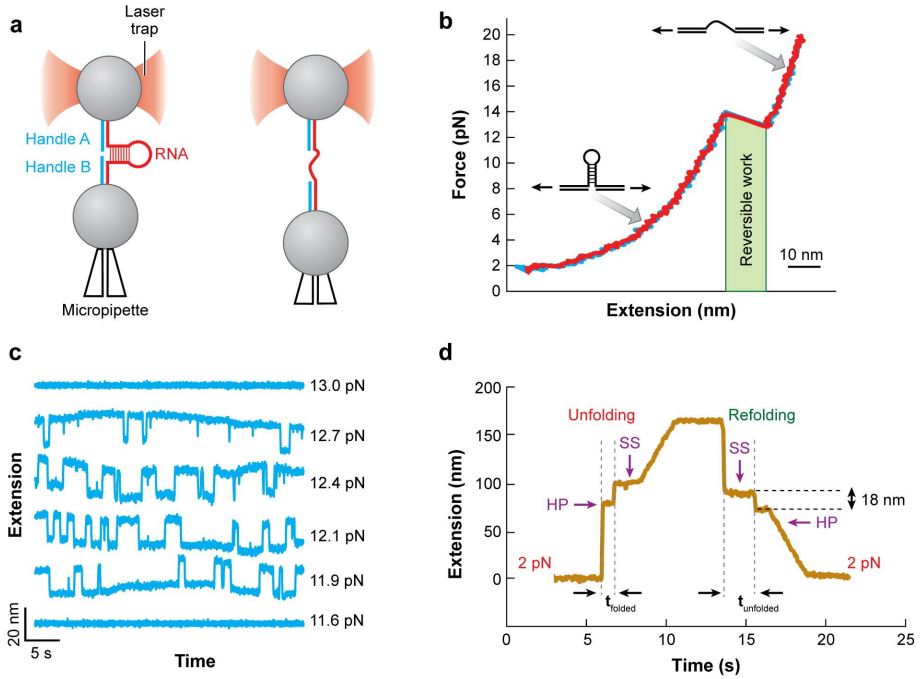




Pollack L. 2011.
Annu. Rev. Biophys. 40:225–42

Optical tweezers

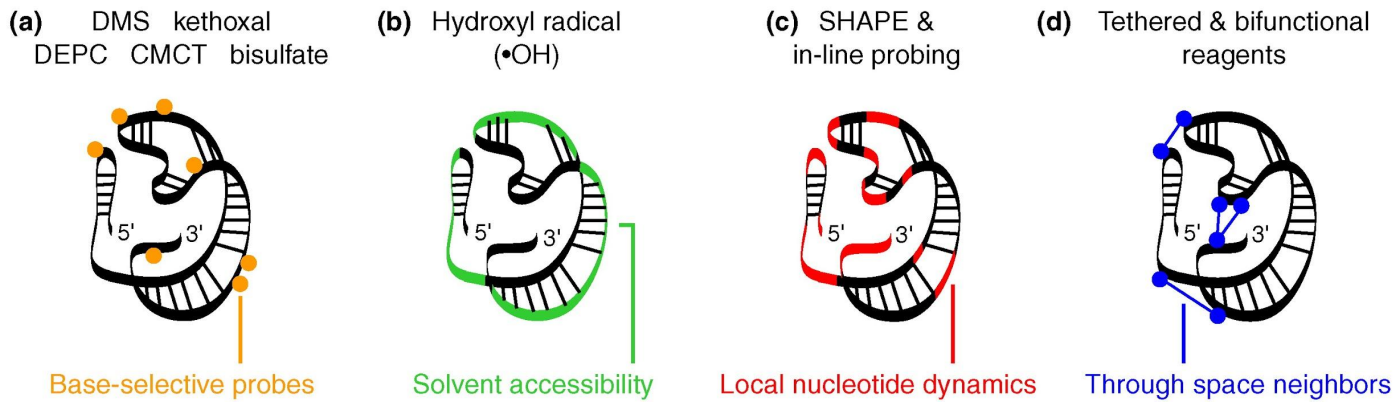
- Force unfolding of RNA structures
- Provide varied useful informations
- Limited by preexisting knowledge of the structure
- Interpretation becomes more difficult with bigger structures



Li PTX, et al. 2008.
Annu. Rev. Biochem. 77:77–100.

Chemical probing

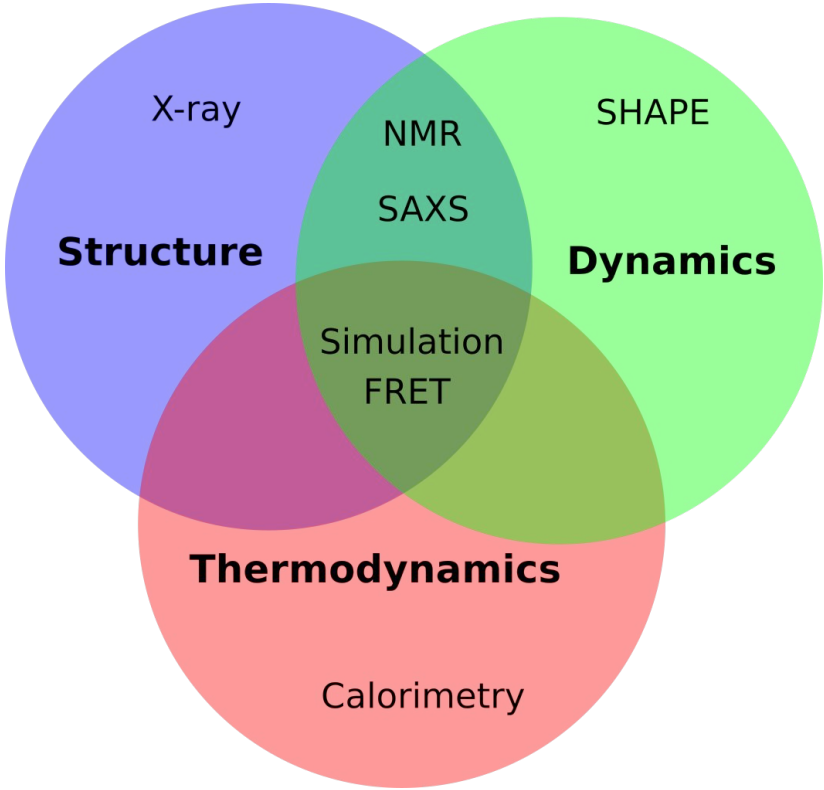
- Fast
- Applicable to any RNA
- No detailed structural data



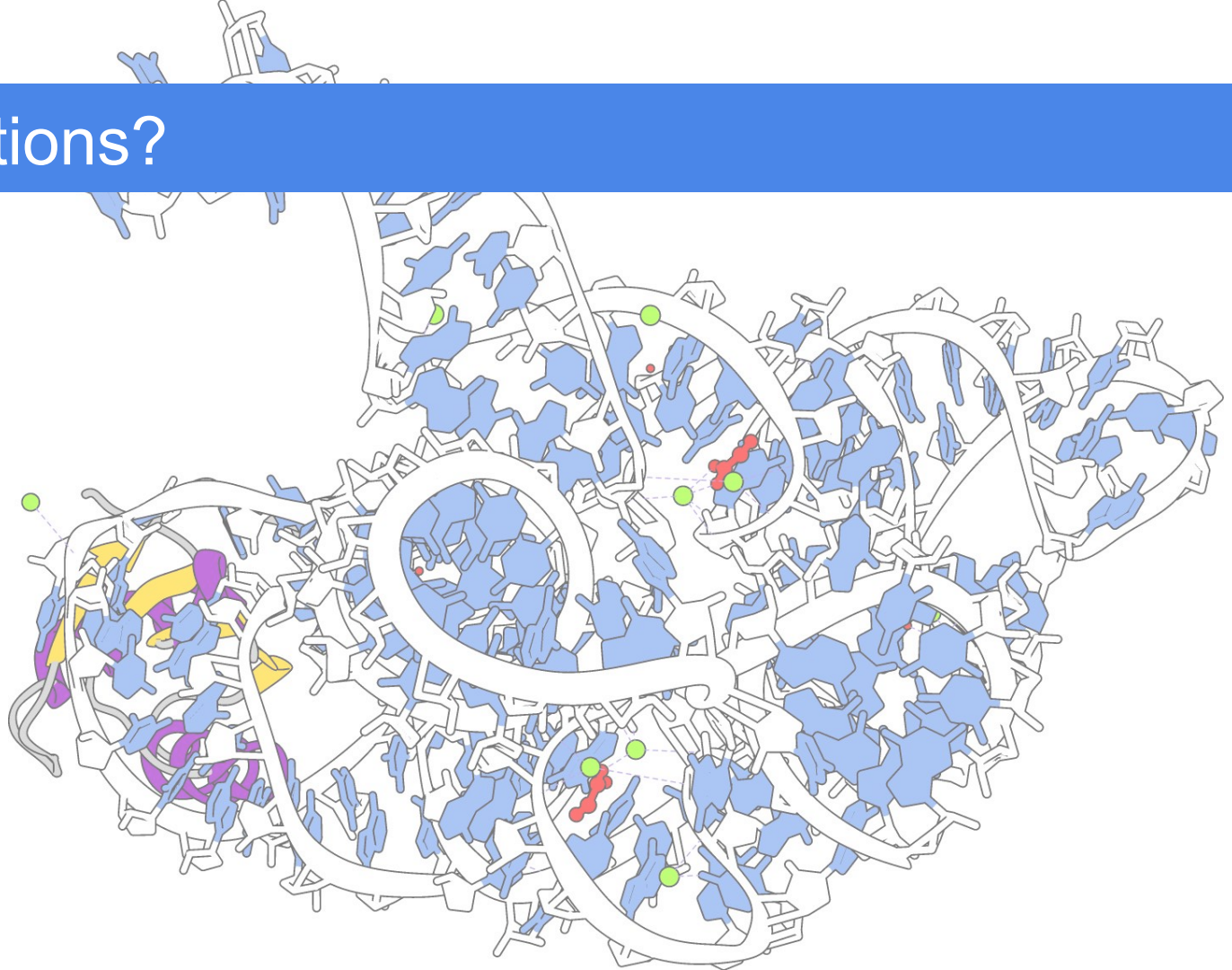
Weeks, Curr. Opin. Struct. Biol., vol. 20, no. 3, pp. 295–304, May 2010. doi:

Various techniques

- More methods: FRET, SANS, CD
- None provide a complete picture of RNA behaviour
- Theory is useful to combine and compare experimental results
- To compare different interpretations of the existing data



Questions?



Visualising structures with Chimera

- Download and install chimera (https://www.cgl.ucsf.edu/chimera/)
- Launch chimera
- Go to File -> Fetch by ID
- Type ‘1KF1’, then click on Fetch
- Presets ->
- Atoms -> Nucleotide representation

Tools -> higher-order structure -> unit cell

Make copies

‘2MBJ’

Visualising structures with Chimera

RNA to try

- Adenine riboswitch: 1Y26
- Telomerase: 2K96
- Encapsidation signal: 1S9S
- tRNA: 6TNA
- Self-splicing group I intron: 1U6B

Make your own

```
rna path 1,39,7,8,30,9 40

rna model UUCAGAGUCUUAUACCAGCUAAGUCCAACAUUUUAUGAGU #0
```

Visualising structures with Chimera

Finding h-bond network

- Fetch the sarcin-ricin loop: 480D
- Presets -> all atoms
- Select -> Structure -> Nucleic acid
- Tools -> Structure analysis -> Find Hbond
- Choose only find h-bonds with **both ends** selected

Do you see ‘forked’ h-bonds? Are those real?

Why is the phosphate-base contact listed as an hbond?

Going further

Eterna: www.eternagame.org

Game based on RNA 2D prediction

FoldIt: www.fold.it

Game based on protein 3D prediction

Thank you