

## Fundamentals of Nucleic Acid Structural Biology

- Nucleic Acids:
  - Definition
  - Building Blocks (Nitrogenous base, Sugar, Phosphates)
- Sugar:
  - Sugar Puckering
    - Differences between Deoxyribose and Ribose
    - C3'-endo and C2'-endo configuration
  - Sugar Numbering
  - Chemical Properties of Sugar positions
  - Why DNA and RNA differs and how the sugar participates in their chemical-physical difference?
    - Glycosidic Bond
    - 2'-C position
    - Furanoses
    - 5'-C position
- Nitrogenous Bases:
  - Purines
    - Imidazole and Pyrimidine subsystem
      - Numbering
  - Pyrimidines:
    - Numbering
- Phosphates
  - How phosphates influence Nucleic Acid Folding?
  - Polyanionic nature of Nucleic Acids
- Nucleotide and Nucleoside definition
  - Sin and Anti conformation
- Nucleic Acid Classes
  - DNA
    - DNA double helix
      - Geometrical Features

- Conformation : (A-DNA, B-DNA, Z-DNA)
    - Biotech Application: Johnson & Johnson DNA Vaccine
    - DNAzymes: DNAMoreDB
  - RNA
    - RNA is a polymorphic and self-folding molecules
    - RNA as a catalyst
    - RNA folding is a hierarchical process
    - Torsional Angles:
      - Alpha
      - Beta
      - Gamma
      - Delta
      - Epsilon
      - Zeta
      - Chi
    - What is the difference between an RNA and DNA double helix?
- Nucleotide – Nucleotide Interactions
  - Edges:
    - Watson Crick edges
    - Hoogsteen edges
    - Sugar edges
      - Proposed Topics:
        - A-minor motifs
        - Ribose-zipper
  - Pairing families and relationships:
    - Isostericity of canonical interactions
    - Non-canonical Interactions
      - Wooble Interaction
  - Stacking Interactions
    - Negative and Positive Stacking Interactions
- Nucleotide modifications:
  - How many natural occurring modifications are currently known?

- Proposed Topic: Modifications and SarsCovid2 Evolution
  - Role of ADAR and APOBEC enzymes: How adenosine to inosine hydrolytic deamination is suggested to influence Covid-19 evolution?
- Structural Properties and molecular roles of:
  - M6A:  $N^6$  – *methyladenosine*
  - D: Dihydrouridine
  - M1A:  $N^1$  – *methyladenosine*
- RNA structural motifs
  - Hairpin Loop
  - Bulge Loop
  - Internal Loop
  - RNA Junction
- RNA Tertiary Interactions:
  - Kissing Loops
  - Pseudoknots
- tRNA structures and modification landscape
- ModeRNA

## SUGGESTED READINGS

Fundamentals of RNA Structure and Function 2022 ISBN : 978-3-030-90213-1 (Chapter 1 – 2)

Suzuki T. The expanding world of tRNA modifications and their disease relevance. *Nat Rev Mol Cell Biol.* 2021 Jun;22(6):375-392. doi: 10.1038/s41580-021-00342-0. Epub 2021 Mar 3. PMID: 33658722

Kim SC, Sekhon SS, Shin WR, Ahn G, Cho BK, Ahn JY, Kim YH. Modifications of mRNA vaccine structural elements for improving mRNA stability and translation efficiency. *Mol Cell Toxicol.* 2022;18(1):1-8. doi: 10.1007/s13273-021-00171-4. Epub 2021 Sep 20. PMID: 34567201; PMCID: PMC8450916.

Ganser LR, Kelly ML, Herschlag D, Al-Hashimi HM. The roles of structural dynamics in the cellular functions of RNAs. *Nat Rev Mol Cell Biol.* 2019 Aug;20(8):474-489. doi: 10.1038/s41580-019-0136-0. PMID: 31182864; PMCID: PMC7656661.

Wu MT, D'Souza V. Alternate RNA Structures. *Cold Spring Harb Perspect Biol.* 2020 Jan 2;12(1):a032425. doi: 10.1101/cshperspect.a032425. PMID: 31896543; PMCID: PMC6942119.

Nikolova EN, Stull F, Al-Hashimi HM. Guanine to inosine substitution leads to large increases in the population of a transient G·C Hoogsteen base pair. *Biochemistry.* 2014 Nov

25;53(46):7145-7. doi: 10.1021/bi5011909. Epub 2014 Nov 10. PMID: 25339065; PMCID: PMC4245982.

Biochemistry Horton-Perry Chapter19 (Until 19.3, excluded)

Andrea Cappannini, Angana Ray, Elżbieta Purta, Sunandan Mukherjee, Pietro Boccaletto, S Naeim Moafinejad, Antony Lechner, Charles Barchet, Bruno P Klaholz, Filip Stefaniak, Janusz M Bujnicki, MODOMICS: a database of RNA modifications and related information. 2023 update, *Nucleic Acids Research*, Volume 52, Issue D1, 5 January 2024, Pages D239–D244, <https://doi.org/10.1093/nar/gkad1083>

Andrea Cappannini, Kevin Mosca, Sunandan Mukherjee, S Naeim Moafinejad, Richard R Sinden, Veronique Arluison, Janusz Bujnicki, Frank Wien, NACDDB: Nucleic Acid Circular Dichroism Database, *Nucleic Acids Research*, Volume 51, Issue D1, 6 January 2023, Pages D226–D231, <https://doi.org/10.1093/nar/gkac829>

Almudena Ponce-Salvatierra, Pietro Boccaletto, Janusz M Bujnicki, DNAmoreDB, a database of DNAzymes, *Nucleic Acids Research*, Volume 49, Issue D1, 8 January 2021, Pages D76–D81, <https://doi.org/10.1093/nar/gkaa867>

Magdalena Rother, Kristian Rother, Tomasz Puton, Janusz M. Bujnicki, ModeRNA: a tool for comparative modeling of RNA 3D structure, *Nucleic Acids Research*, Volume 39, Issue 10, 1 May 2011, Pages 4007–4022, <https://doi.org/10.1093/nar/gkq1320>

Leontis NB, Stombaugh J, Westhof E. The non-Watson-Crick base pairs and their associated isostericity matrices. *Nucleic Acids Res.* 2002 Aug 15;30(16):3497-531. doi: 10.1093/nar/gkf481. PMID: 12177293; PMCID: PMC134247.

Westhof E. Isostericity and tautomerism of base pairs in nucleic acids. *FEBS Lett.* 2014 Aug 1;588(15):2464-9. doi: 10.1016/j.febslet.2014.06.031. Epub 2014 Jun 17. PMID: 24950426.

Laing C, Schlick T. Analysis of four-way junctions in RNA structures. *J Mol Biol.* 2009 Jul 17;390(3):547-59. doi: 10.1016/j.jmb.2009.04.084. Epub 2009 May 13. PMID: 19445952; PMCID: PMC2777522.