Overview RNA Resources and Tools December 10, 2003

RNA has been part of the central dogma of molecular biology for years. Its structural role in protein synthesis as part of the ribosomal complex and its participation as the mediator of amino acid transfer in protein synthesis have been to well described. RNAs can form complicated secondary folds and stable three dimensional shapes. This in turn can allow specific binding of substrates and even catalytic functions. A number of catalytically competent ribozymes have been described (Lilley, 2003; Steitz & Moore 2003). The dual functionality of RNA, that is, the ability to form precise structures with catalytic function and the capacity for reproduction have logically lead to speculation regarding the potential role of RNA in the pre-biotic Darwinian soup (Spirin, 2002).

In the last several years the additional role in intron editing has become more prominent and recent advances have pointed to the roles of small RNA oligos siRNA miRNA in control of expression have begun to emerge. The use of RNA interference (RNAi) for manipulation of gene expression has nearly reached the clinical stage (Check 2003). Non-coding RNAs act purely at the level of the RNA. Each class of non-coding RNA is encoded by a relatively small number of genes (a few tens to a few hundred at most. Lim LP et al 2003).
Examples of non-coding RNAs include:

- Small RNAs (snRNA, snoRNA, gRNA) - Involved in the splicing of immature RNAs into final active form (mRNA, tRNA, rRNA) including the formation of 2'-O-methylated and pseudouridine bases in appropriate locations.
- Guide RNAs (gRNAs) - Structural RNAs that help stabilize the macromolecular complexes involved in editing of immature RNAs.
- Ribosomal RNAs (rRNAs) - Structural and catalytic components of ribosomes, which are composed of several types of rRNA and about 100 different proteins.
- Transfer RNA (tRNA) - Adaptor molecules that bring amino acids to the mRNA/ribosome complex.
- Transfer-Messenger RNAs (tmRNAs) - Performs a dual task in bacterial protein translation in adding a degradation signal peptide to the end of undesirable or damaged gene products. This also rescues the 70s ribosome which was stalled on the defective message.
- Antisense RNA and RNAi - Expressed short pieces of RNA (ss or ds) that result in prevention
of protein synthesis.
Small cytosolic RNAs (scRNAs) - Involved in protein trafficking

- **Ribozymes** - Catalytic RNAs that can selectively bind to a substrate and catalyze a large and increasing number of reactions.

RNA is generally a single-stranded molecule that can form a much greater variety of complex three-dimensional molecular shapes than double-stranded DNA. Therefore, it can perform a greater variety of functions.

![Diagram](http://people.musc.edu/~hazards/WebBioInformatics/RNA_analysis.htm)

Fig. 1. A model for the molecular steps in RNA silencing.
Introduction/Scope

Coding RNAs are derived from the transcription of DNA into messenger RNA (mRNAs) which encodes sequence information to be translated into a protein.

They also exist in the form of viral genomes encoded as vRNA.
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<th>(+) ssRNA</th>
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<td>Moloney murine leukemia virus (MMLV)</td>
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<td>Feline Leukemia virus</td>
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**Virology Net**

**Diseases and Viruses at CDC**

**NCBI Viral Genomes**

**Influenza Database, HIV Search Page**

**Viral Informatics**

**GtRDB, tRNA scan**

**Organelle Based**

**Mito1 Strasbourg**

**NCBI Organelles**

**GOBase**

**MitoMap**

**Noncoding RNAs**

**European ribosomalRNA**

**5SRNA**
16S RNA

Ribosomal Database RNA

RISCC Ribosomal Internal Spacer Sequence Collection Note the use of RISC for the complex which cleaves targetted mRNA in RNAi processes.

Small RNAs

Invitrogen on how RNAi works, Ambion on how RNAi works, Dharmacon

Small RNAs database

uRNA/snRNA database

snoRNA, Yeast snoRNA

tmTRNA trNA-mRNA duel types

tmRDB

RNAi database at NYU

Ambion

RNA modification

RNA editing

Consequences of RNA structure?
What you see below is a limitation of most protein viewers. That is they do not simultaneously do nucleic acids very well. This is 1FFK 50S ribosome.
FirstView: 1ffk

Protein Explorer © 2002 by Eric Martz

- **Rotate** the molecule by dragging on it with the mouse. *Print the 1-Hour Tour*
- **Chains**: Each chain of protein, DNA, or RNA is shown in a different color as a **backbone trace**.
- **Ligands**: When present, ligands, metals, carbohydrate, **water**, etc. (**hetero atoms**) are spheres colored to identify the elements:
  
  C | H | O | N | P | S | Fe  
  (More elements)

- **Disulfide bonds**, when present, are shown between backbone traces, **sulfur-colored**.
- **Identify** any atom by clicking on it, noting the report in the window below.

1ffk Molecule Information

**Explore More with QuickViews!**
- **1-Hour Tour** · Help/Index/Glossary
- Form for Recording Observations
- Viewer of 3D Structural Data · Quit

# Commands May Be Entered Here

**Commands:** Back Fwd  Messages: Clear Control  Options

64281 atoms selected!
select all
spacefill
No atoms selected!
select water

64281 atoms selected!
select all
spacefill off
No atoms selected!

** Show Aliases  Preferences  Force Ready  Set Project Folder

Document: Done
Prokaryotic Translation: Coupled transcription-translation allows for secondary structures to affect transcription rates, translation rates and termination of both.

Eukaryotic Translation: Secondary structure is known to influence translation initiation and elongation rates…a key feature in antisense and RNAi inhibition is accessibility of the target region (exposed loops within 2º Structure).

- Catalysis (e.g., ribosomes, spliceosomes)
RNA Structure Links

**RNABase**

**NDB Rutgers**

**RCSB, NCBI MMDB, SCOR**

A paper by **Collier AJ et al 2002**
Structure Prediction

Looking for UTR features (e.g., Internal Ribosome Entry Site IRES) in your sequence. UTRScan, PatScan

Trying to locate potential miRNA or siRNA binding sites is not a straightforward BLAST/FASTA problem. The short query lengths and the potential for mismatches render the guiding statistics of BLAST/FASTA insensitive. The Zuker Group and the Pearson Lab (note the RNA check box for query type in the LALIGN form) among others are developing tools for such applications.

Zuker Mfold
RNAStructure

Sean Eddy Lab COVE, RNABOB, PKNOTS

Vienna RNA

RNAdraw

SStructView

Non-canonical Base Pair Database
NON-CANONICAL BASE PAIR DATABASE: Individual Record Page 1072

Authors: Cate JH, Gooding AR, Podell E, Zhou K, Golden BL, Kundrot C

Citation: Crystal structure of a group I ribozyme domain: principles of RNA catalysis. Nature 273(5628):1678-85 September 20, 1994

Base Pair Type: AA amino-N3 (1 bond)

Base Pair Category: Single Hydrogen Bond Mismatches; Cis Watson-Crick/Shallow

Sequence Context: 5' 3'
A-A, N3-amino
A-A
A-U*
3' 5'

Structure: Group I Intron

Pucker Info: A206 C2'endo, A114 C3'endo

Melting Point: *

Free Energy: *

Chemical Shift: *

Glycosidic Conf: A206 syn, A114 anti

Extra Info: A114.A206 form a mismatch

Figure:
### Organism: Tetrahymena thermophila

### Abbreviation: Tt-LSU_P3/P7

### RNA type: Ribozymes

### Keywords: self-splicing; long distance interaction; Ciliophora

### EMRL number: V01416

### Submitted by: A.F.Gultyaev (sgultyaev@rulsfb.leidenuniv.nl)

### Supported by: Crystal structure; Mutagenesis; Sequence comparison; Structure probing

### References:

### Comment:
The Tetrahymena ribozyme is the representative structure of group I introns (for review see structure of the introns, deduced from comparative analysis [2], is mainly in agreement with [3].

The numbering is according to the EMBL database entry (V01416): the 5'-end position 147 corresponds to the position 96 in the full-length intron.

Non-Watson-Crick contacts, identified in the crystal structure [3], are:
- U152 * U1324 (U101 * U73 in full-length intron numbering, stem P3);
- A155 * A321 (A104 * A270, stem P3);
- G330 * A350 (G279 * A299, stem P8);
- A320 * A357 (A269 * A306, stem P7).

### Stem sizes: 7 6
### Loop sizes: 158 2 28

### Position Paired:
- 147–151; 325–329
- 153–154; 322–323
- 331–337; 343–349
- 313–314; 363–363
- 315–319; 358–362

### Bracket view of structure:

![Bracket view of structure](http://people.musc.edu/~hazards/WebBioInformatics/RNA_analysis.html)

### Comparative RNA
(Once you complete their registration you can retrieve things like this)
**Secondary Structure: small subunit ribosomal RNA**

**Xenopus laevis**
(M27605)

1. Eukaryota 2. eucautyte crown group
3. Fungi/Metazoa group 4. Metazoa
23. Xenopus

January 2000

Citation and related information available at http://www.rna.icmb.utexas.edu

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**Some references**

Search [NAR by RNA categories](http://people.musc.edu/~hazards/WebBioInformatics/RNA_analysis.html).


Carrington and Ambros. The role of MicroRNAs in Plant and Animal Development *Science 301:336*.
2003


Shi Y. Mammalian RNAi for the masses. *Trends Genetics* 19(1):9-12


Zeng Y et al. MicroRNAs and small interfering RNAs can inhibit mRNA expression by similar mechanisms. *PNAS* 100(17): 9779-9784.

Zeng Y and Cullen BR. Sequence requirements for micro RNA processing and function in human cells. *RNA* 2003:112-123.

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A worked Example

See the sample questions CASP7 does not fit well into the RNA world as a query.

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Sample Questions/Data

- Use the NCBI ENTREZ server to find mitochondrial myopathy and mRNA to locate some RefSeq entries.
- Use the NCBI ENTREZ server to find tRNA structures.
- Find a 3D structures for a hammerhead ribozyme, an IRES region, and the A site of a 50S ribosome.
- Find a 3D structure model for a Triple Base Interaction as, for example, for AAA. (HINT try the non-canonical base link, scan the non-interactive page click more info to see an entry).
- Find the small subunit (SSU) rRNA secondary structure model of Chlamydomonas reinhardtii. (HINT: try RNA WWW server click on secondary structure, then select the species.)
- How closely related are green algae and red algae based on small subunit rRNA sequences?
- What kind of RNA modifications can be found in snRNA of Eukarya? (HINT RNA modifications site)