

*Part II - Applications of MultiSeq
Evolution of Translation: Dynamics of
Recognition in RNA:Protein Complexes*

Zaida (Zan) Luthey-Schulten

Dept. Chemistry, Physics, Beckman Institute, Biophysics, Institute of Genomics

Biology

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NIH Center Macromolecular Modeling and
Bioinformatics

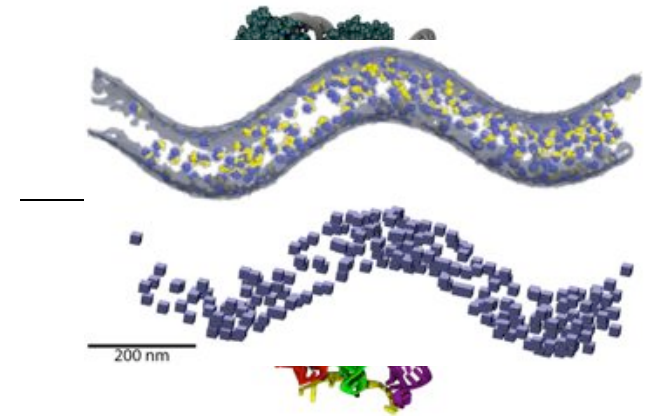
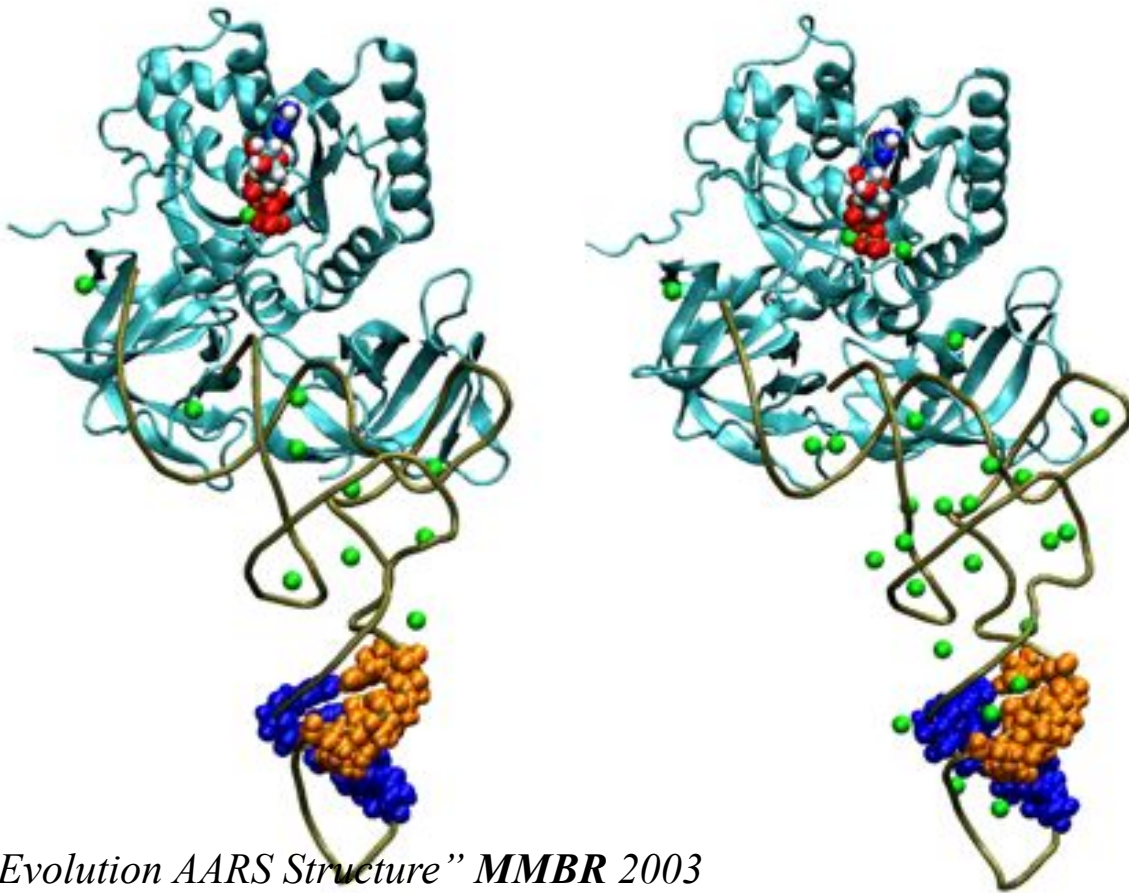


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Protein:RNA Complexes in Translation

Evolution, Dynamics, Analysis



**Proteins/RNA
Polyribosomes
Ribosome**

“Evolution AARS Structure” *MMBR* 2003

“Evol. Profiles Class I&II AARS” *JMB* 2005

“Evolution SepRS/CysRS” *PNAS* 2005

“Dynamic Signaling Network” *PNAS* 2009

“Exit Strategy Charged tRNA” *JMB* 2010

“Mistranslation in Mycoplasma” *PNAS* 2011

“Dynamical Recognition Novel

Amino Acids” *JMB* 2008

“tRNA Dynamics” *FEBS* 2010

“Signatures ribosomal evolution”

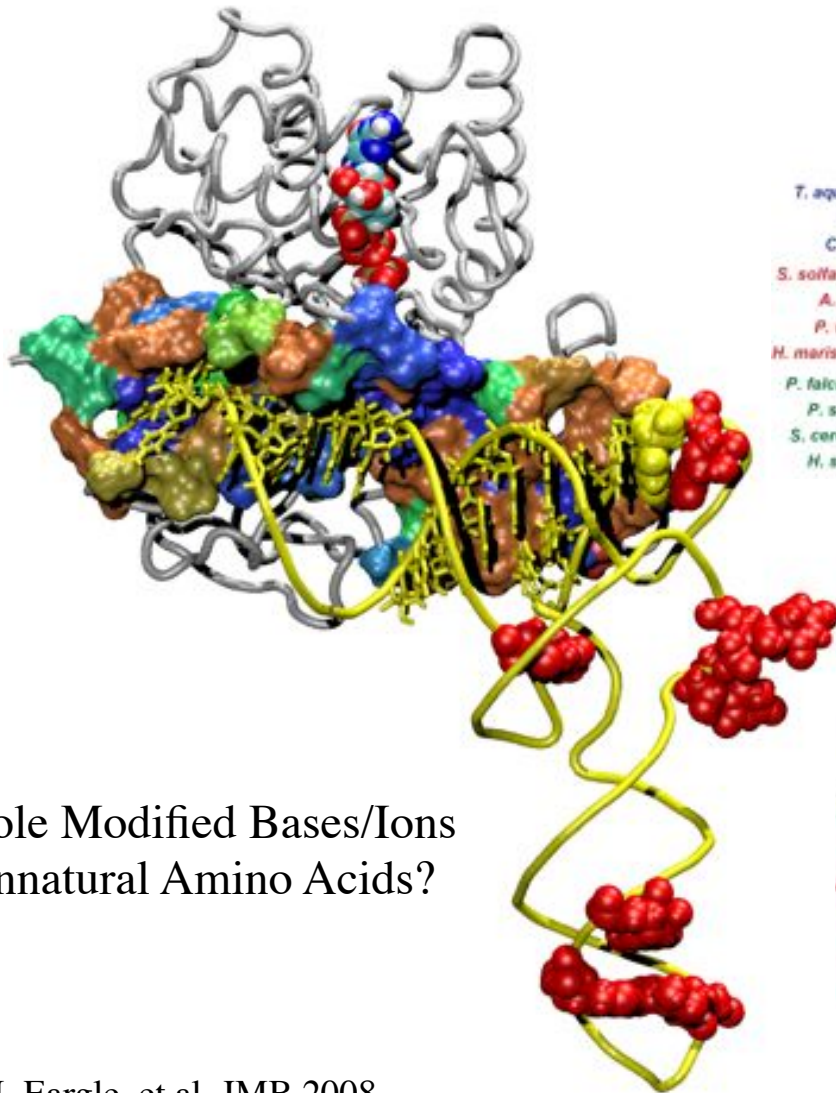
PNAS 2008, *BMC* 2009, *BJ* 2010

“Motion L1 Stalk:tRNA” *JMB* 2010

“Whole cell simulations on GPUs”

IEEE 2009, *Plos CB* 2011, *PRL* 2011

Evolution of Protein/RNA Interfaces: Dynamics of EF-Tu/tRNA Recognition



| | Switch I | | | | | Switch II | | | | | Domain II | | | | | | | | | | | | | | | | | | | | | | | |
|------------------------|----------|---|---|---|----|-----------|---|---|---|---|-----------|-----|---|---|---|---|---|---|---|---|---|---|---|-----|---|---|---|---|---|---|---|---|---|----------|
| | 50 | + | + | * | 57 | 85 | * | • | * | • | 92 | 224 | * | | | | | | | | | | | 240 | | | | | | | | | | |
| <i>T. aquaticus</i> | I | D | K | A | P | E | E | R | H | A | D | V | I | K | N | M | P | V | E | D | V | F | T | I | T | G | R | G | T | V | A | T | G | B |
| <i>E. coli</i> | I | D | N | A | P | E | E | K | H | A | D | V | V | K | N | M | P | I | E | D | V | F | S | I | S | G | R | G | T | V | V | T | G | A |
| <i>C. jejuni</i> | I | D | N | A | P | E | E | K | H | A | D | V | V | K | N | M | P | I | E | D | V | F | S | I | S | G | R | G | T | V | V | T | G | E |
| <i>S. solfataricus</i> | L | D | R | L | K | E | E | R | H | R | D | F | V | K | N | M | P | I | G | D | V | V | S | I | S | G | V | G | T | V | P | V | G | |
| <i>A. pernix</i> | L | D | K | M | K | E | E | R | H | R | D | F | V | K | N | M | P | V | Q | N | V | V | S | I | P | G | A | G | T | V | P | V | G | |
| <i>P. woesei</i> | M | D | R | L | R | E | E | R | H | R | D | F | V | K | N | M | P | I | G | D | V | V | S | I | K | G | V | G | T | V | P | V | G | |
| <i>H. marismortui</i> | M | D | N | L | A | E | E | R | H | R | D | F | V | K | N | M | P | I | G | D | V | V | T | I | S | G | I | G | T | V | P | V | G | |
| <i>P. falciparum</i> | L | D | K | L | K | A | E | R | H | K | D | F | I | K | N | M | P | L | G | D | V | V | K | I | G | G | I | G | T | V | P | V | G | |
| <i>P. sativum</i> | L | D | K | L | K | A | E | R | H | R | D | F | I | K | N | M | P | L | G | D | V | V | K | I | G | G | I | G | T | V | P | V | G | |
| <i>S. cerevisiae</i> | L | D | K | L | K | A | E | R | H | R | D | F | I | K | N | M | P | L | Q | D | V | V | K | I | G | G | I | G | T | V | P | V | G | |
| <i>H. sapiens</i> | L | D | K | L | K | A | E | R | H | R | D | F | I | K | N | M | P | L | Q | D | V | V | K | I | G | G | I | G | T | V | P | V | G | |

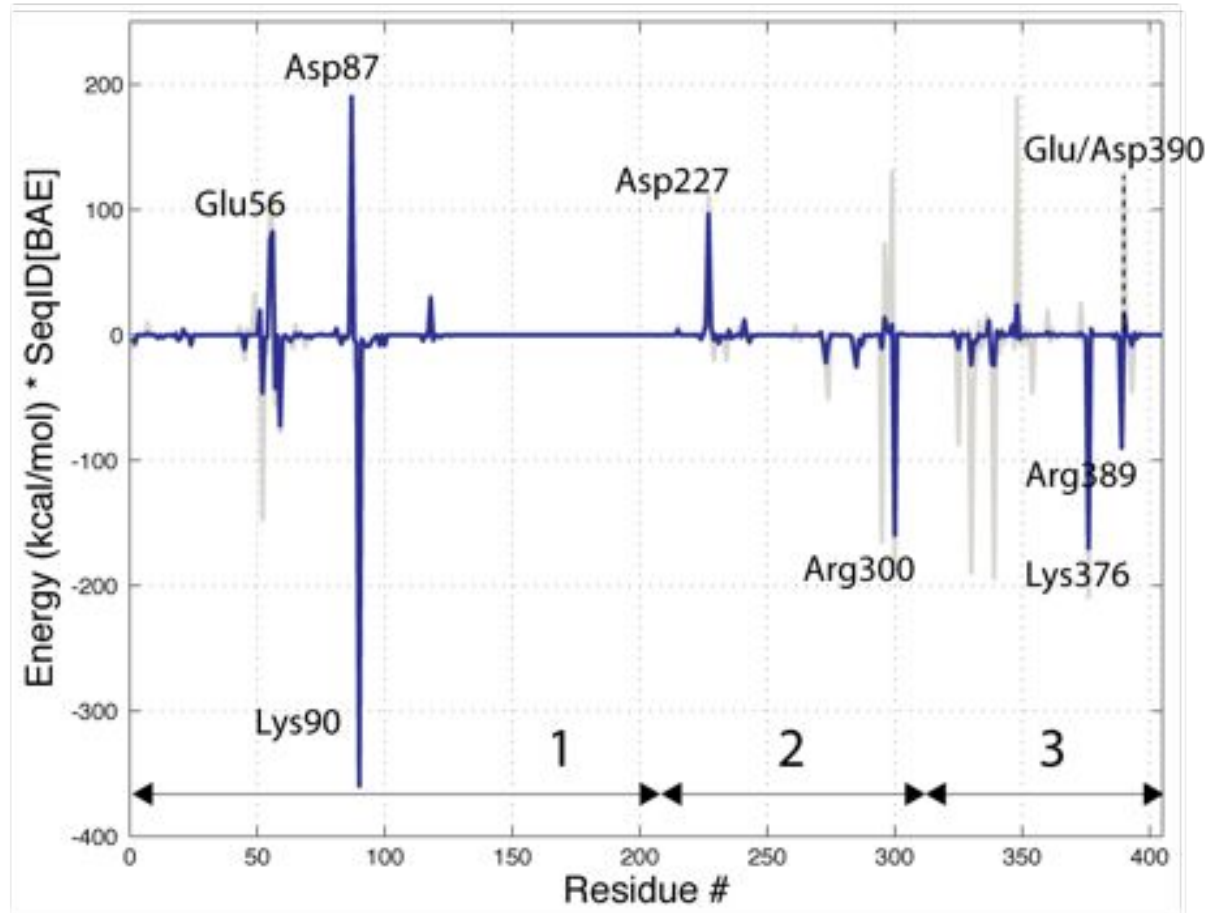
| | Domain II | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|------------------------|-----------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----|---|---|---|---|---|---|---|----------|----------|
| | 271 | | | | | | | | | | | | | | | | | | | • | + | + | * | 302 | | | | | | | | | |
| <i>T. aquaticus</i> | E | N | H | R | K | T | L | G | E | G | I | A | G | D | N | V | G | L | L | R | G | V | S | R | E | E | V | E | R | G | G | B | |
| <i>E. coli</i> | E | N | F | R | K | L | L | D | E | G | R | A | G | E | N | V | G | V | L | L | R | G | I | K | R | E | E | I | E | R | G | D | A |
| <i>C. jejuni</i> | E | N | F | R | K | E | M | D | Q | G | E | A | G | D | N | V | G | V | L | L | R | G | T | K | K | E | E | V | I | R | O | M | E |
| <i>S. solfataricus</i> | E | T | H | H | T | K | M | D | K | A | E | P | G | D | N | I | G | F | N | V | R | G | V | E | K | K | D | I | K | R | G | D | |
| <i>A. pernix</i> | E | N | H | Y | Q | Q | L | Q | A | E | P | G | D | N | I | G | F | A | V | R | G | V | S | K | S | D | I | K | R | G | D | | |
| <i>P. woesei</i> | E | N | H | H | E | P | L | E | E | A | L | P | G | D | N | I | G | F | N | V | R | G | V | S | K | H | D | I | K | R | G | D | |
| <i>H. marismortui</i> | E | N | H | H | E | E | V | P | K | A | E | P | G | D | N | V | G | F | N | V | R | G | V | G | K | D | D | I | R | R | G | D | |
| <i>P. falciparum</i> | E | N | H | X | E | V | L | E | E | A | R | P | G | D | N | I | G | F | N | V | K | N | V | S | V | K | E | I | K | R | G | V | |
| <i>P. sativum</i> | E | N | H | H | E | A | L | T | E | A | L | P | G | D | N | V | R | F | N | V | K | N | V | A | V | K | D | L | K | H | C | L | |
| <i>S. cerevisiae</i> | E | N | H | H | E | Q | L | E | Q | D | V | P | G | D | N | V | G | F | N | V | K | N | V | S | V | K | E | I | R | R | G | N | |
| <i>H. sapiens</i> | E | N | H | H | E | A | L | S | E | A | L | P | G | D | N | V | G | F | N | V | K | N | V | S | V | K | D | V | R | R | G | N | |

Role Modified Bases/Ions
Unnatural Amino Acids?

Dynamical Recognition EF-Tu/tRNA (E.coli)

Combining MD with Evolutionary Analysis (MultiSeq)

Non-bonded Interaction Energy

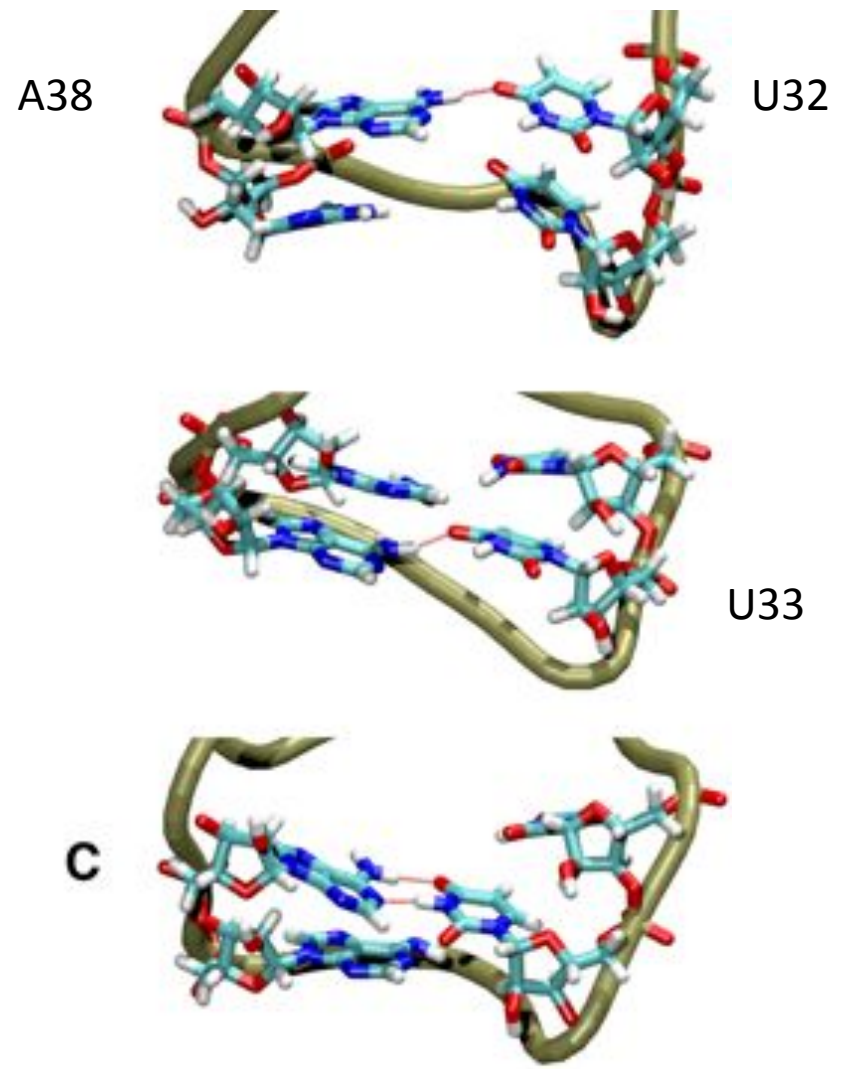
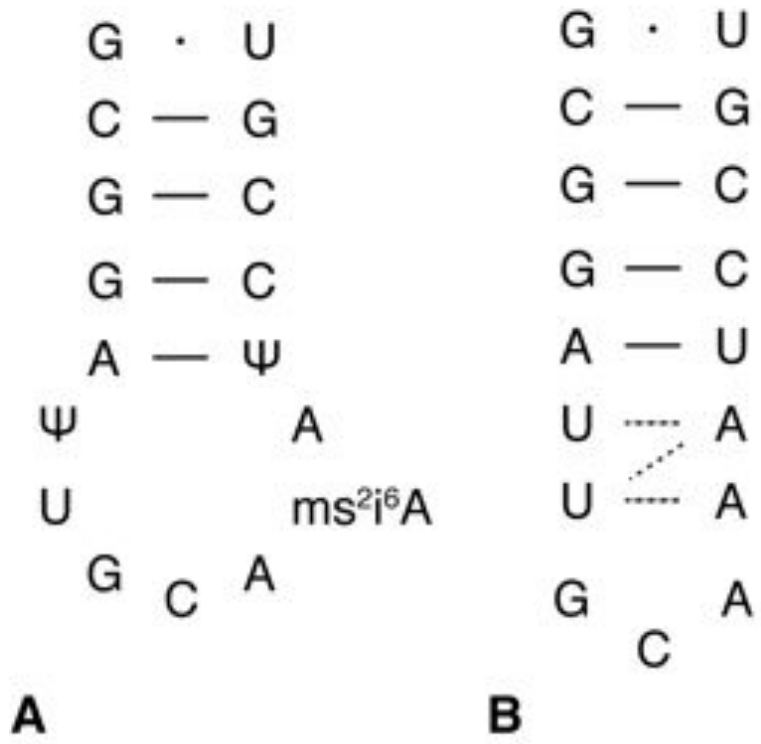


BAE

*J. Eargle, A. Sethi, A. Black, L. Trabuco & Z. Luthey-Schulten. JMB
“Dynamics of Recognition in EF-Tu/tRNA Complex” (2008)*

Effects of Modified Bases on Dynamics of AC Stem/Loop

MD simulations of unmodified tRNA:Cys



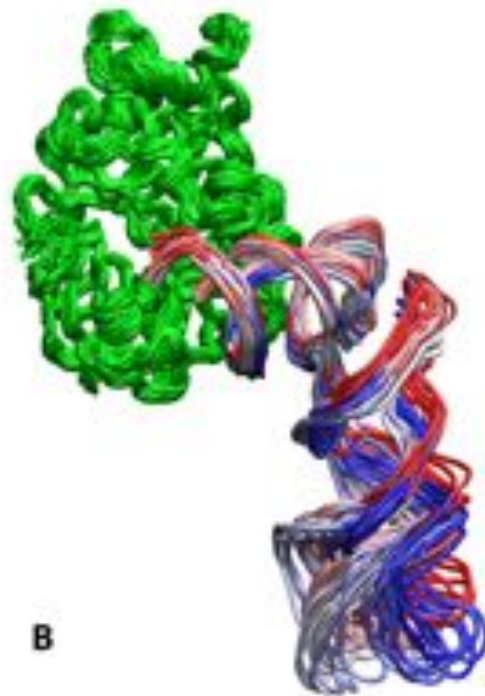
Similar NMR structures for unmodified tRNA-Phe
 Nikonowicz, *JMB* 2002, *personal communication*

Eargle, et al. *JMB* (2008))

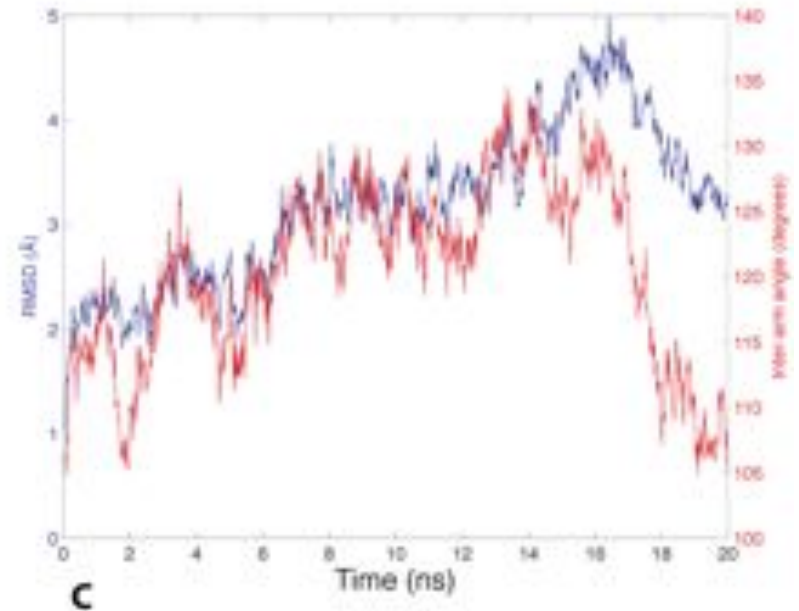
Flexibility in tRNA structures observed in crystallography and simulations



X-ray 5 tRNAs



MD EF-Tu:tRNA:cys

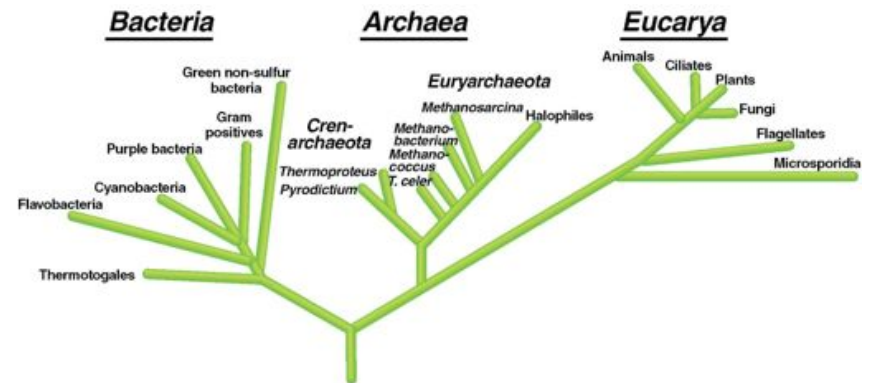
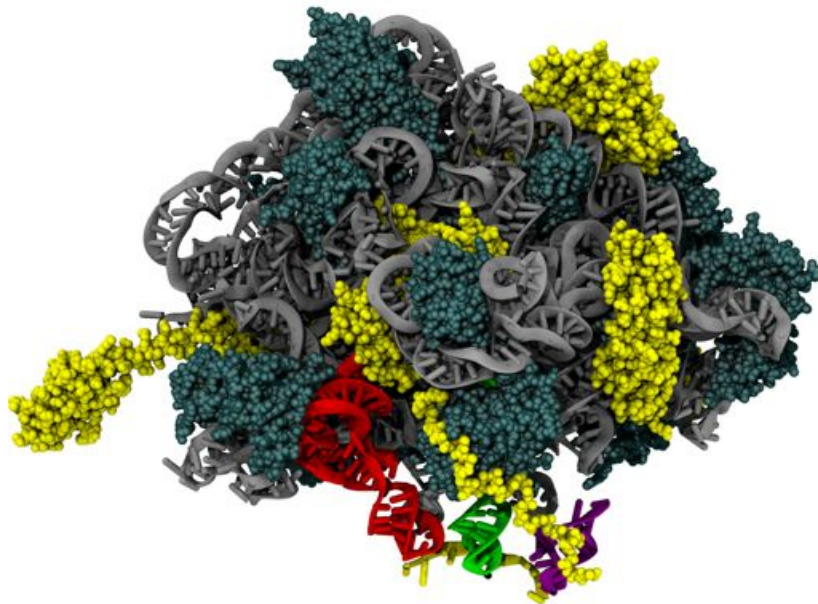


MD: RMSD and Interarm Angle in tRNA:cys

Molecular Signatures in Ribosome Evolution

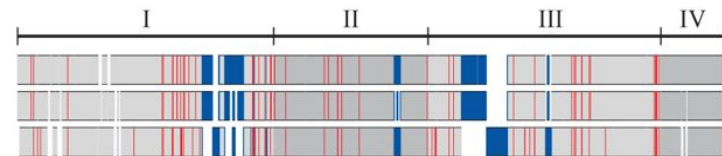
Archaeal - LSU

Universal Phylogenetic Tree



16S rRNA

E. coli
T. thermophilus
H. marismortui



Dynamical function of ribosomal signatures: idiosyncrasies in ribosomal RNA and/or proteins characteristic of the domains of life

Roberts, Sethi, Montoya, Woese, Luthey-Schulten (2008) *PNAS* 105:13953

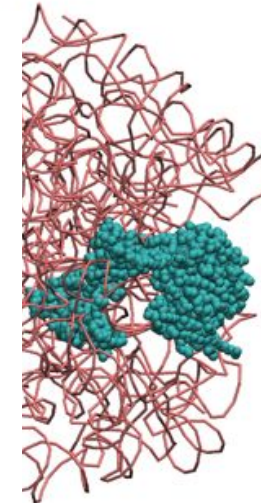
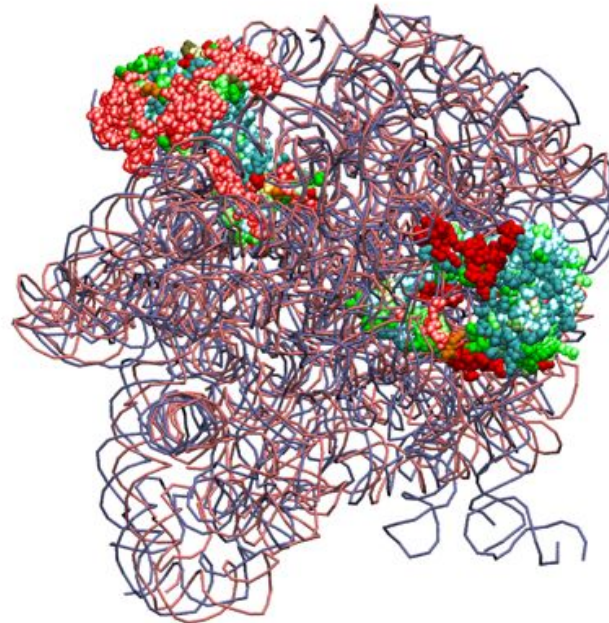
Chen, Eargle, Sarkar, Gruebele, Luthey-Schulten (2010) *Biophysical Journal*

Structural Overlaps with STAMP

Comparing ribosomal large subunit with r-proteins L2 and L3
 180,000 atoms in 4 rRNAs and 58 proteins



E. coli



arismortui

| Sequence Name | 50 | 60 | 70 | 80 | 90 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|--|----|----|----|----|----|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 23S rRNA | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| <input type="checkbox"/> 2aw4_B | A | U | G | A | A | B | A | C | B | U | B | C | U | A | A | B | B | B | U | C | B | B | U | A | A | B | B | U | G | A | | | | | | | | | | | |
| <input type="checkbox"/> 1s72_0 | C | A | A | G | C | U | B | C | G | A | A | A | G | C | C | A | U | G | G | G | A | G | C | C | G | C | A | C | G | G | A | G | A | | | | | | | | |
| 5S rRNA | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| <input checked="" type="checkbox"/> 2aw4_A | U | C | K | G | A | A | B | U | B | A | A | C | B | C | C | U | A | B | C | C | C | B | A | U | B | | | | U | F | B | U | B | U | B | G | B | | | | |
| <input checked="" type="checkbox"/> 1s72_9 | A | C | B | G | A | A | B | U | B | A | A | C | B | C | C | U | A | B | C | C | C | B | A | U | B | | | | U | F | B | U | B | U | B | G | B | | | | |
| Ribosomal Protein L2 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| <input type="checkbox"/> 2aw4_C | | | | G | R | N | H | N | G | R | I | T | I | R | H | I | G | D | G | H | K | G | A | Y | R | I | V | D | F | K | R | N | K | D | | | G | I | P | A | |
| <input type="checkbox"/> 1s72_A | R | G | T | S | T | F | | | | | | | | R | A | | | | | P | S | H | R | Y | K | A | D | L | E | H | R | K | V | E | D | G | D | V | I | A | G |
| Ribosomal Protein L3 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| <input type="checkbox"/> 2aw4_D | M | T | R | I | F | T | | | | | | | | E | D | G | V | S | I | P | V | T | V | I | E | V | E | A | N | R | V | T | Q | V | K | | | | | | |
| <input type="checkbox"/> 1s72_B | T | H | V | V | L | V | N | D | E | F | N | S | P | R | E | G | M | E | E | T | V | P | V | T | V | I | E | T | P | P | M | R | A | V | A | L | R | A | Y | E | D |

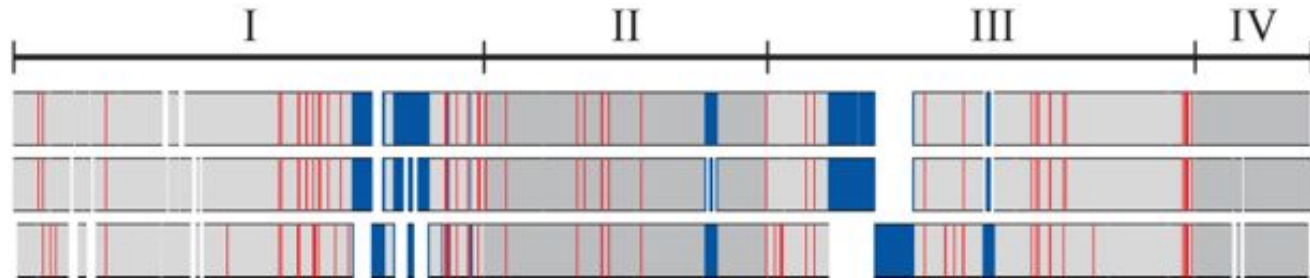
Sequence and Structure Signatures in Ribosomal RNA

16S rRNA

E. coli

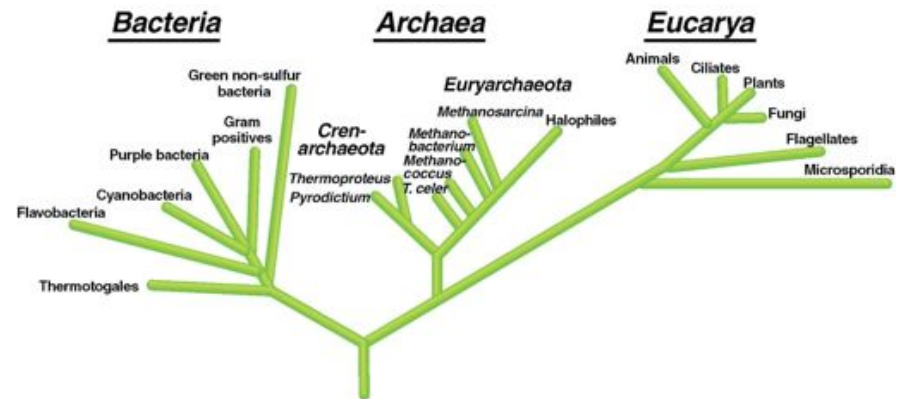
T. thermophilus

H. marismortui



Ribosomal Signatures: Idiosyncrasies in rRNA and/or rproteins characteristic of the domains of life

69 (119) & 6 (14) in 16S (23S)

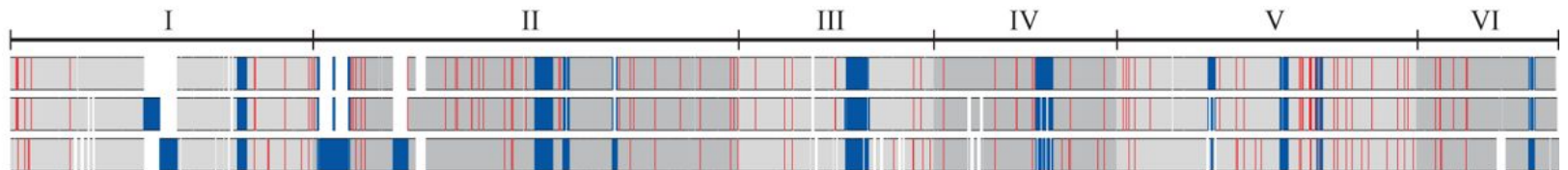


23S rRNA

E. coli

T. thermophilus

H. marismortui



Signature analysis

- Signatures are sequence and/or structural features that are characteristic of a domain of life*.
- Identify the sequence signatures in the 16S rRNA and proteins using MultiSeq
- **MultiSeq has a coloring based on signatures**, but use Scripts to collect quantitative data about the signatures: position, composition.
- **Signature analysis can be applied to any set of sequences/groupings**

* E. Roberts, A. Sethi, J. Montoya, C. Woese, Z Luthy-Schulten (2008) *PNAS*

Signature analysis script

```
proc get_taxa_signatures {args} {

  initializeMultiSeqEnvironment

  # Load the alignment.
  set sequenceIDs [::SeqData::Fasta::loadSequences $alignmentFilename]

  # Find the reference species.
  set refSequenceIDs {}
  foreach species $referenceSpecies {
    set found 0
    foreach sequenceID $sequenceIDs {
      if {[string toupper [::SeqData::getScientificName $sequenceID]] == [string toupper $species]} {
        lappend refSequenceIDs $sequenceID
        set found 1
        break
      }
    }
  }

  # Group the sequence ids.
  array set groupData {names {}}
  foreach sequenceID $sequenceIDs {

    set group ""
    if {$rankName == "domain"} {
      set group [::SeqData::getDomainOfLife $sequenceID]
    } else {
      set group [::SeqData::getLineageRank $sequenceID $rankName]
    }
    if {![info exists groupData($group)]} {
      lappend groupData(names) $group
      set groupData($group) {}
    }
    lappend groupData($group) $sequenceID
  }
}
```


Signature analysis script (cont)

```
# Calculate the signatures for the groups.
set signatures [::SeqEdit::Metric::Signatures::calculateSignatures $sequenceGroups $groupConsensusCutoff \
               $otherGroupMaxCutoff $otherGroupMaxGapFraction $maxConservedBlockDistance $minConservedBlockSize]

# Print the signatures.
puts ""
puts "Ordered Signatures"
printSignatureHeader $groups $refSequenceIDs
for {set position 0} {$position < [llength [lindex $signatures 0]]} {incr position} {

    # Get the signature for each of the groups.
    set isSignature 0
    for {set groupIndex 0} {$groupIndex < [llength $groups]} {incr groupIndex} {
        set groupSignature [lindex [lindex $signatures $groupIndex] $position]
        if {[string length $groupSignature] == 1} {
            set isSignature 1
        }
    }

    if {$isSignature} {
        printSignatureLine $position $groups $refSequenceIDs $signatures $sequenceGroups
    }
}
}
```

Signature analysis script (cont)

```
proc getCompositionString {sequenceIDs position} {  
  # Go through each group to count the elements.  
  array set counts {values {}}  
  foreach sequenceID $sequenceIDs {  
    set element [::SeqData::getElement $sequenceID $position]  
    if {![info exists counts($element)]} {  
      lappend counts(values) $element  
      set counts($element) 1  
    } else {  
      incr counts($element)  
    }  
  }  
  
  set ret ""  
  foreach element $counts(values) {  
    set percentage [expr round(100.0*double($counts($element))/double([llength $sequenceIDs]))]  
    if {$percentage > 5} {  
      if {$ret != ""} {  
        append ret "/"  
      }  
      append ret "${element}($percentage\%)"  
    }  
  }  
  
  return $ret  
}
```

Signature script output

Ordered Signatures

| Pos | E._coli | T._therm | H._maris | Archaea | Bacteria |
|------|---------|----------|----------|----------------------|---------------------------|
| 35 | 33 | 33 | 27 | U(28%)/C(72%) | *A(96%) |
| 42 | 39 | 39 | 33 | *U(100%) | *G(95%) |
| 51 | 47 | 47 | 42 | *G(97%) | C(85%)/U(7%)/G(8%) |
| 59 | 53 | 53 | 49 | *C(100%) | A(83%)/G(14%) |
| 222 | 113 | 106 | 87 | *C(100%) | *G(95%) |
| 661 | 248 | 243 | 227 | *G(97%) | C(75%)/G(9%)/U(11%) |
| 749 | 314 | 309 | 293 | *G(100%) | *C(97%) |
| 753 | 317 | 312 | 296 | *G(97%) | *U(91%)/G(7%) |
| 777 | 338 | 333 | 317 | *G(97%) | A(89%)/N(9%) |
| 779 | 339 | 334 | 318 | *G(97%) | *C(98%) |
| 780 | 340 | 335 | 319 | *C(94%) | *U(92%)/A(6%) |
| 790 | 349 | 344 | 328 | G(86%)/N(11%) | *A(92%) |
| 791 | 350 | 345 | 329 | C(67%)/U(19%)/N(11%) | *G(98%) |
| 800 | 358 | 353 | 337 | *G(100%) | *U(91%)/C(7%) |
| 802 | 359 | 354 | 338 | *C(97%) | G(59%)/U(9%)/C(9%)/A(20%) |
| 804 | 361 | 356 | 340 | *C(94%) | G(84%)/A(14%) |
| 809 | 365 | 360 | 344 | *A(92%)/U(8%) | *U(97%) |
| 811 | 367 | 362 | 346 | C(83%)/G(14%) | *U(97%) |
| 823 | 377 | 372 | 356 | C(89%)/U(11%) | *G(92%) |
| 833 | 386 | 381 | 365 | *G(94%) | C(89%)/U(6%) |
| 840 | 393 | 388 | 372 | G(83%)/C(14%) | *A(97%) |
| 851 | 403 | 398 | 382 | *A(100%) | C(89%) |
| 920 | 447 | 441 | 416 | C(31%)/U(67%) | *G(92%) |
| 990 | 487 | 471 | 424 | G(89%)/A(8%) | *A(91%) |
| 1083 | 508 | 491 | 446 | *A(97%) | *U(92%) |
| 1085 | 510 | 493 | 448 | *G(97%) | *A(97%) |
| 1087 | 512 | 495 | 450 | *C(92%)/U(8%) | *U(97%) |
| 1089 | 514 | 497 | 452 | *G(92%)/N(6%) | C(89%)/U(8%) |
| 1101 | 523 | 506 | 461 | *C(94%)/A(6%) | *A(96%) |
| 1119 | 537 | 520 | 475 | *C(100%) | *G(91%)/A(8%) |
| 1121 | 539 | 522 | 477 | *G(92%)/A(6%) | A(89%)/G(10%) |
| 1134 | 549 | 532 | 487 | *U(94%) | *C(99%) |

Draw signature figure

- Want to create a graphical representation of the signatures.
- Can use the TCL graphics object to draw figures.

```
proc draw_one_d_alignment {args} {  
  
    # Load the alignment.  
    set alignment [::SeqData::Fasta::loadSequences $alignmentFilename]  
    set numberSequences [llength $alignment]  
    set numberPositions [::SeqData::getSeqLength [lindex $alignment 0]]  
    puts "Loaded $numberSequences sequences of length $numberPositions"  
  
    # Create the drawing canvas.  
    set canvasWidth [expr $draw(xBorder)+($numberPositions*$draw(positionWidth))+$draw(xBorder)]  
    set canvasHeight [expr $draw(yBorder)+($numberSequences*$draw(sequenceHeight))+(($numberSequences-1)*\  
                                                                    $draw(sequenceSpacing))+$draw(yBorder)]  
  
    set g [canvas .drawing -width $canvasWidth -height $canvasHeight]  
  
    # Draw the alignment.  
    for {set i 0} {$i < $numberSequences} {incr i} {  
        set sequenceID [lindex $alignment $i]  
        set y1 [expr $draw(yBorder)+($i*($draw(sequenceHeight)+$draw(sequenceSpacing)))]  
        set y2 [expr $y1+$draw(sequenceHeight)]  
        drawSequencePositions $g $draw(xBorder) $y1 $y2 $sequenceID 0 [expr $numberPositions-1] \  
                                                                    $draw(positionWidth) $draw(sequenceColor) $draw(borderColor) $draw(borderWidth)  
    }  
  
    # Save the canvas.  
    $g postscript -x 0 -y 0 -width $canvasWidth -height $canvasHeight -file $outputFilename  
  
    cleanupMultiSeqEnvironment  
}
```


Draw signature figure (cont)

```

proc drawSequencePositions {g x y1 y2 sequenceID firstPosition lastPosition positionWidth sequenceColor borderColor
                           borderWidth}
{
  set startPosition ""
  for {set j $firstPosition} {$j <= $lastPosition} {incr j} {
    set element [::SeqData::getElement $sequenceID $j]

    # If this is the beginning of a sequence block, record that one started.
    if {$element != "-" && $startPosition == ""} {
      set startPosition $j
    }

    # If this is the end of a sequence block, draw the block.
    if {($element == "-" || $j == $lastPosition) && $startPosition != ""} {
      if {$element == "-"} {
        set endPosition [expr $j-1]
      } else {
        set endPosition [expr $j]
      }
      set x1 [expr $x+($startPosition*$positionWidth)]
      set x2 [expr $x+((($endPosition+1)*$positionWidth)]
      $g create rectangle $x1 $y1 $x2 $y2 -fill $sequenceColor -outline $sequenceColor -width $borderWidth
      $g create line $x1 $y1 $x2 $y1 -fill $borderColor -width $borderWidth
      $g create line $x1 $y2 $x2 $y2 -fill $borderColor -width $borderWidth
      set startPosition ""
    }
  }
}

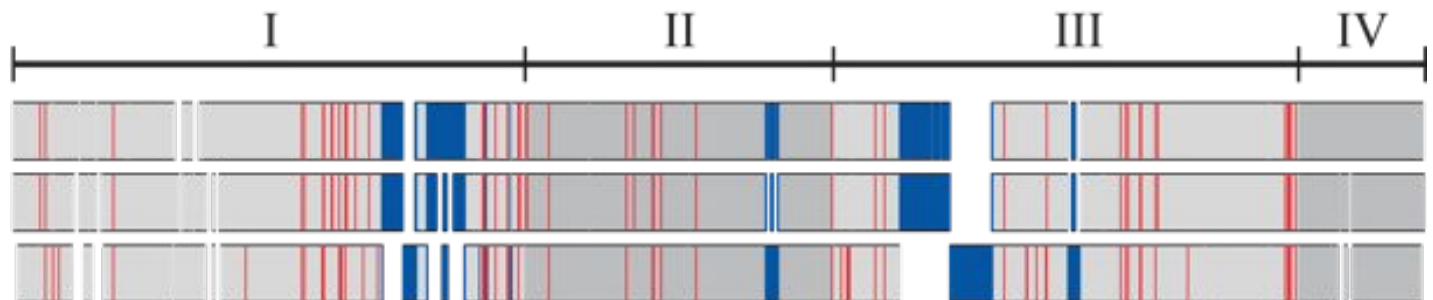
```

16S rRNA

E. coli

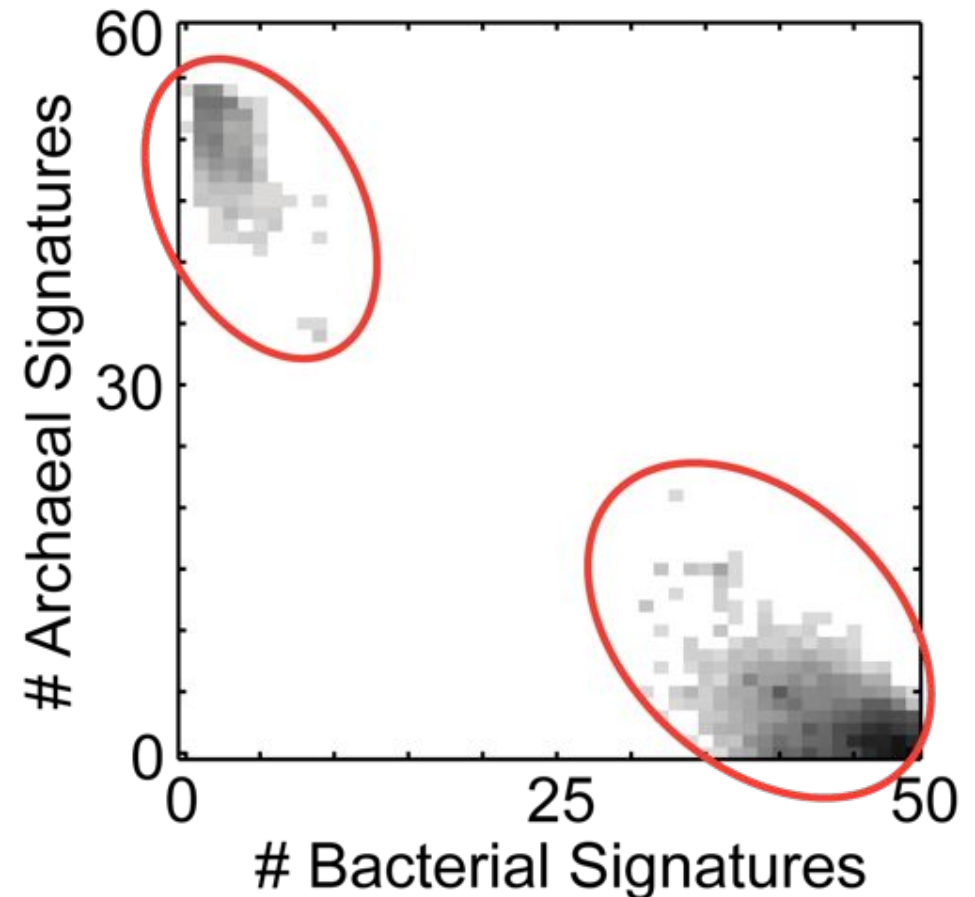
T. thermophilus

H. marismortui

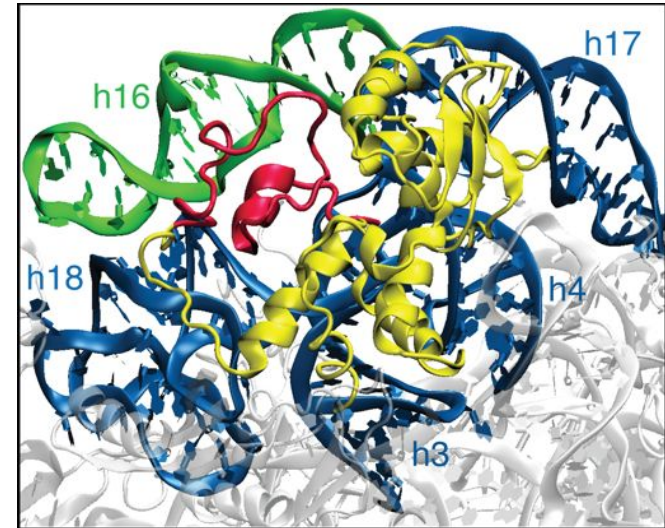
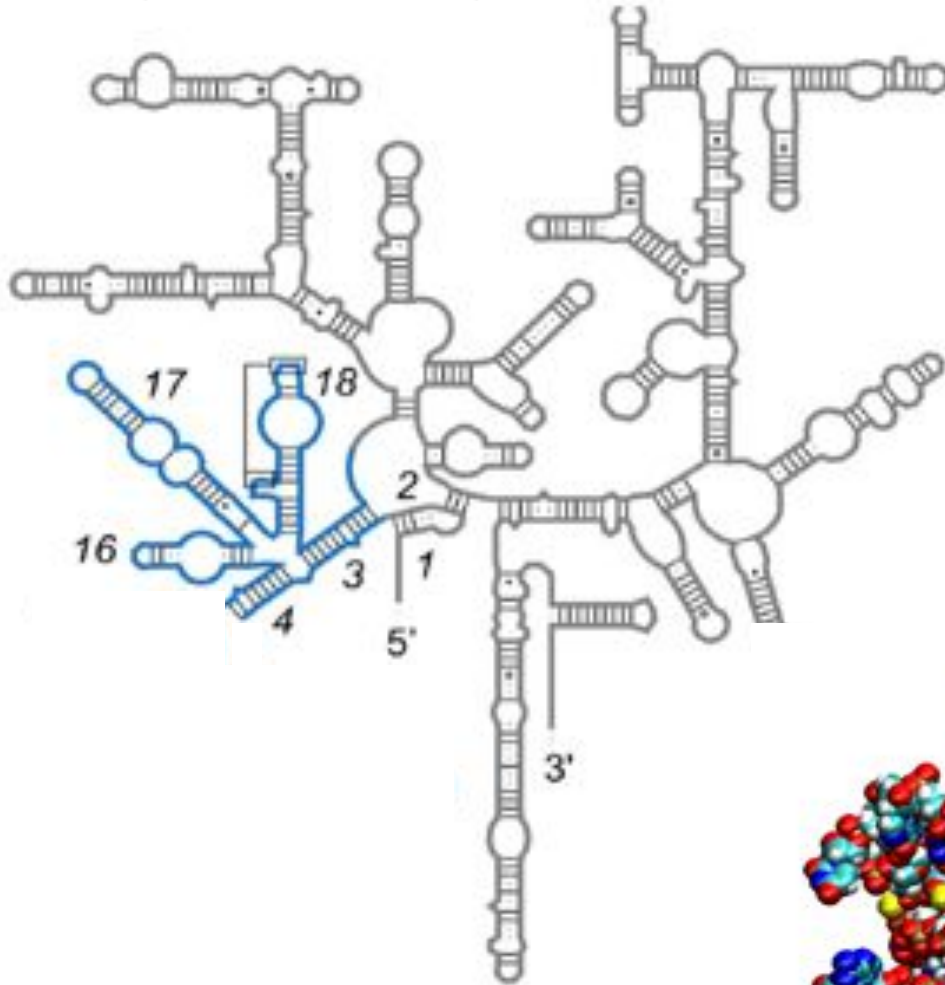


90,000 Environmental 16S rRNA Distinct A & B Sequence Signatures

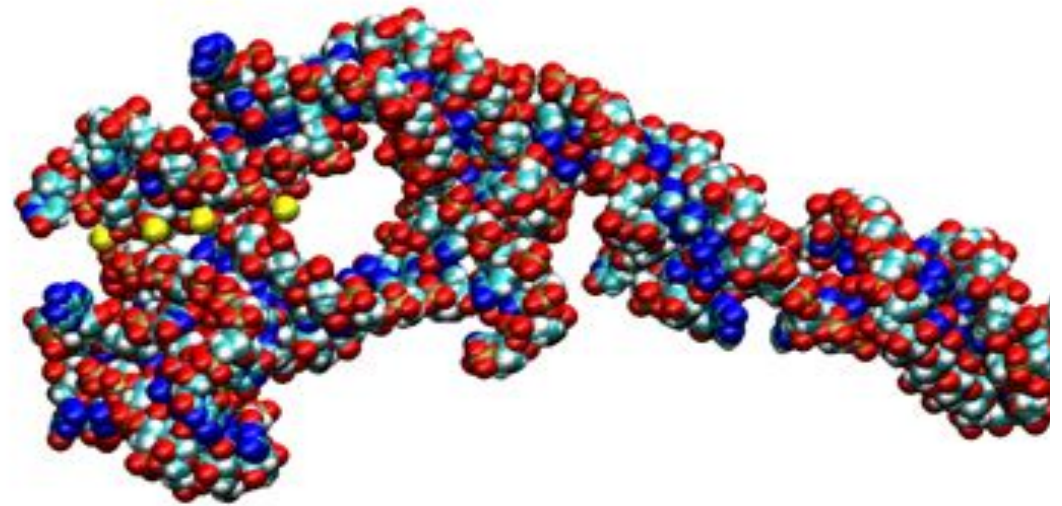
- Analysis of the ribosomal signatures in 90,000 new environmental samples shows that no “gray” area exists: a ribosome is either bacterial or archaeal in nature.
- Split across cluster: 10,000 sequence on each node



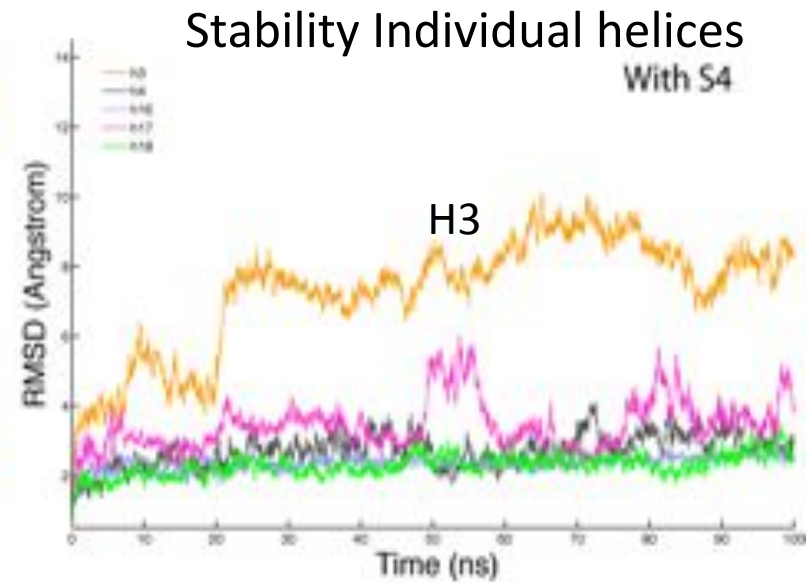
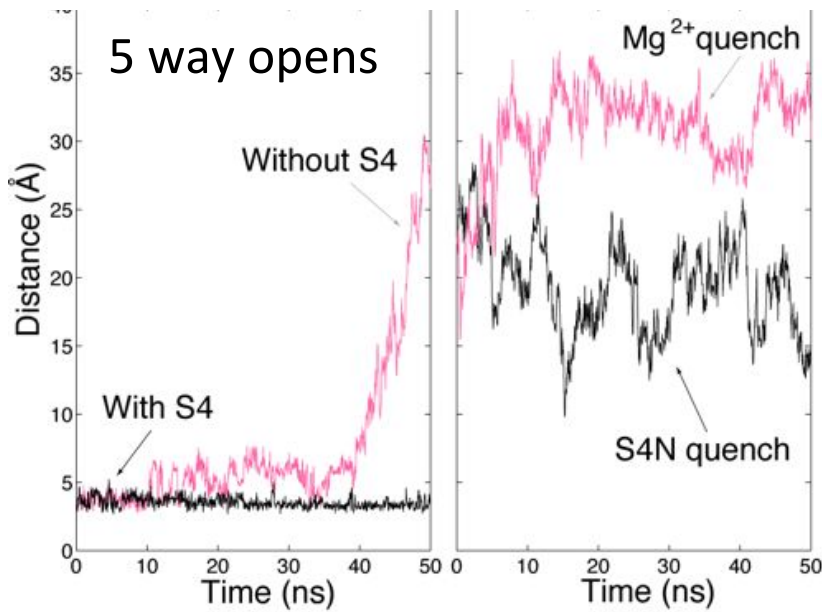
Largest signature region in the SSU



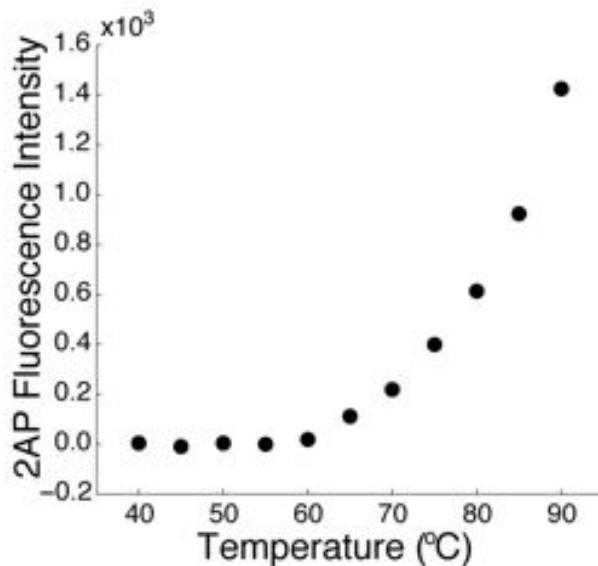
5-way helical junction rRNA with S4



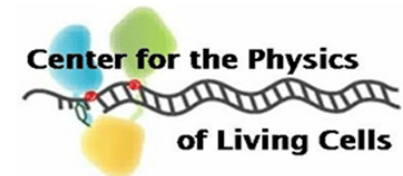
Stability of 5-way junction helices with/without S4



h16 scaled fluorescence

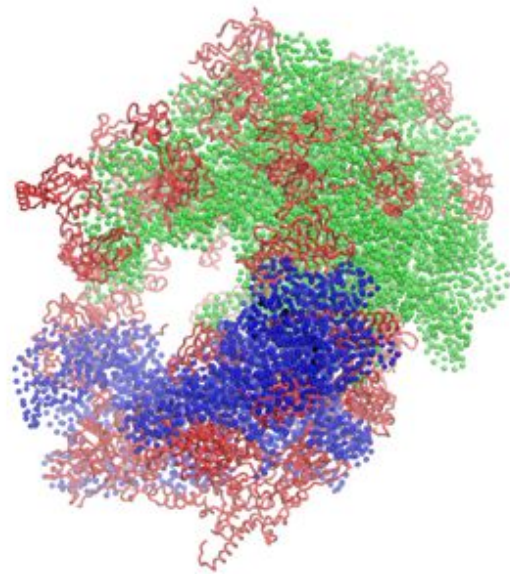


Model for Assembly ?

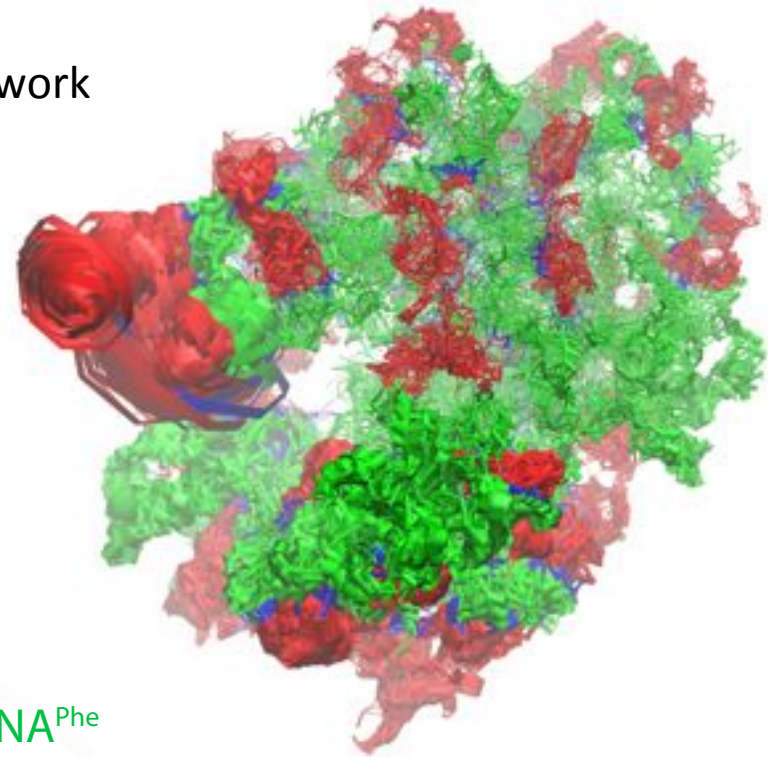


Collaboration with Gruebele, Ha, Woodson labs

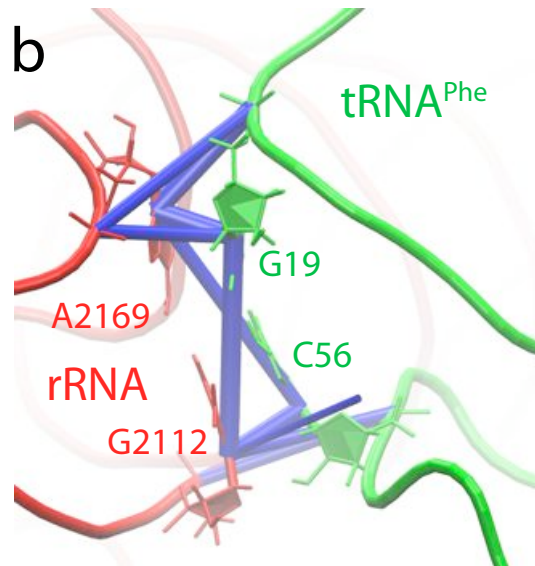
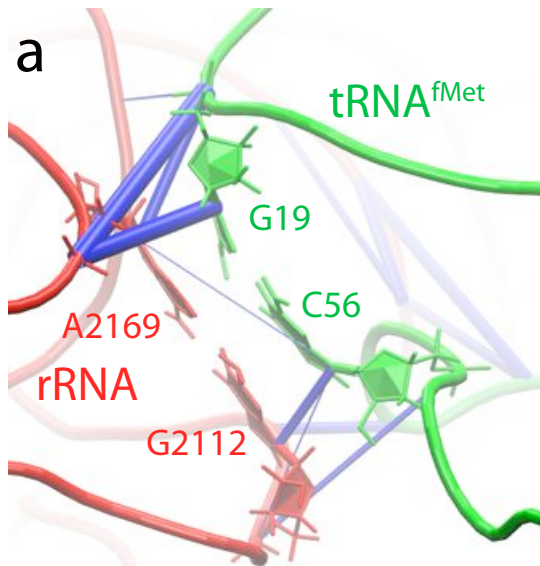
Signaling Networks in LSU & S5U



MD 140ns network



P/E site tRNA:rRNA network



L. Trabuco, E. Schreiner, J. Eargle
et al. JMB 2010

VMD/MultiSeq Tutorials

1. Evolution of Translation: AARS:tRNA
2. Evolution of Translation: EF-Tu:tRNA
3. Evolution of Translation: Ribosome
4. Dynamical Network Analysis - new

Molecular Dynamics Simulations

MD performed with NAMD2 (1) - System Setup

Simulation Parameters

Minimization: 290,000 steps

Production run: 108 ns

Forcefields: CHARMM27 (2), AMBER
(3)

Time step: 1 fs

VdW frequency: 2 fs

VdW cutoff: 12 Å

Switching distance: 10 Å

Pair list distance: 14 Å

Particle Mesh Ewald

Full electrostatic update: 4 fs

Ensemble: NPT

Langevin temperature: 298.15 K

Langevin pressure: 1 atm

Periodic boundary conditions

Contents of System(4)

GluRS

Glu-tRNA^{Glu}

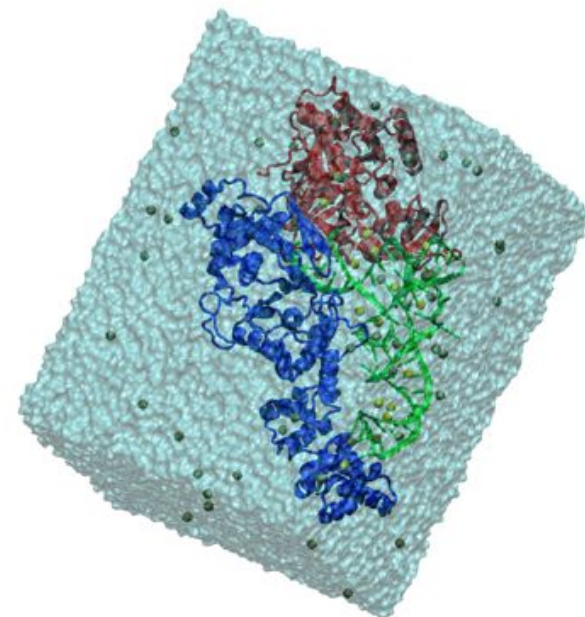
EF-Tu

GTP

Ions: Mg²⁺, K⁺

H₂O: ~27,000 molecules

System: ~130,000 atoms



System Perturbations

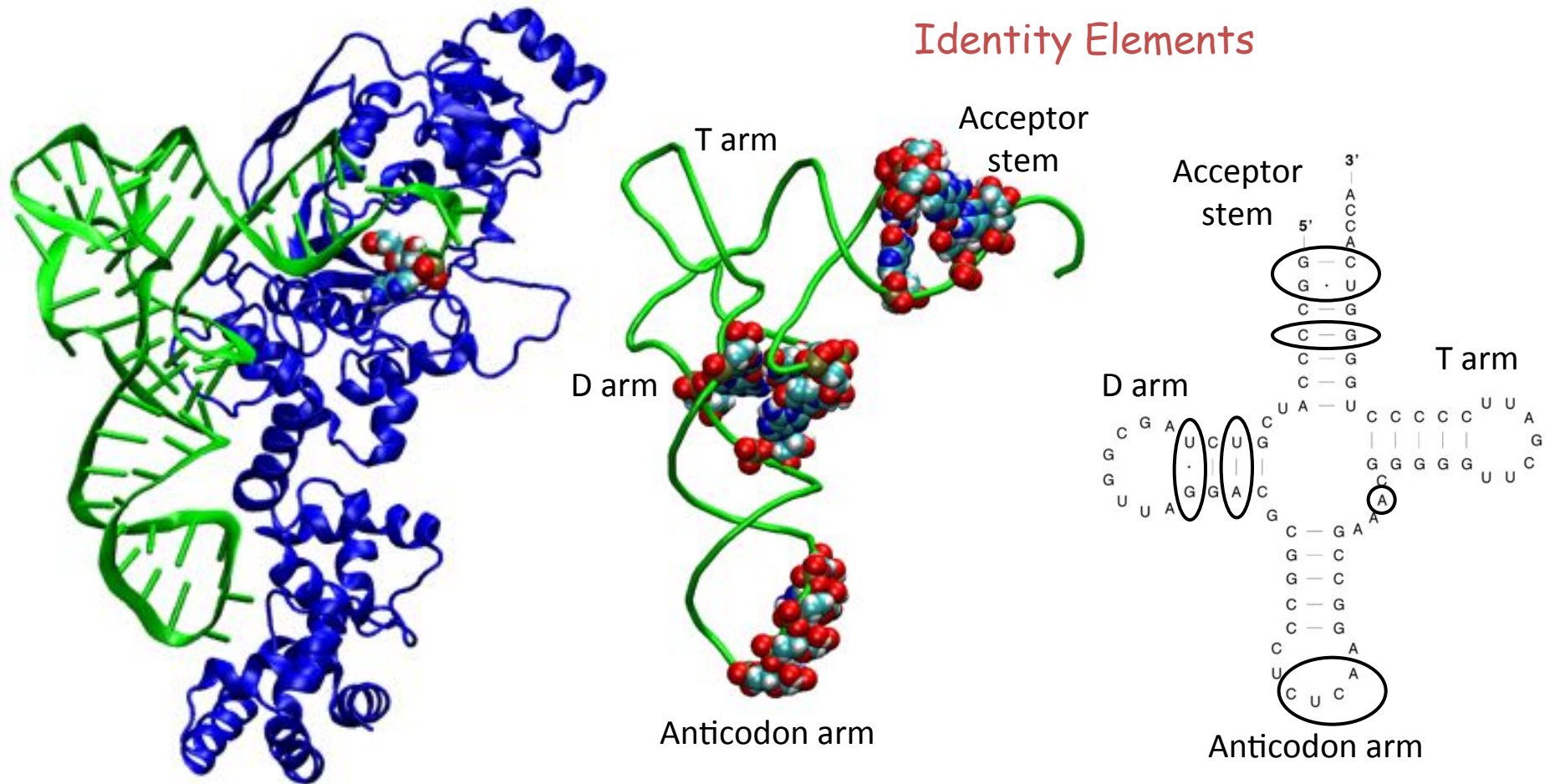
Deprotonation/protonation of reactants (aa,NTs)

Changing rotamer states of residues (5)

involved in long-lived salt bridges

- (1) Phillips, J.C. et al. *J. Comput Chem*, (2005);
- (2) MacKerell, A. et al. *Biopolymers* (2001);
- (3) Case, D. et al. *J. Comput. Chem.* (2005);
- (4) Eargle, J. et al. *JMB* 2010, *FEBS Let.* 2010;
- (5) Dunbrack Jr. and Cohen. *Protein Sci.* (1997)

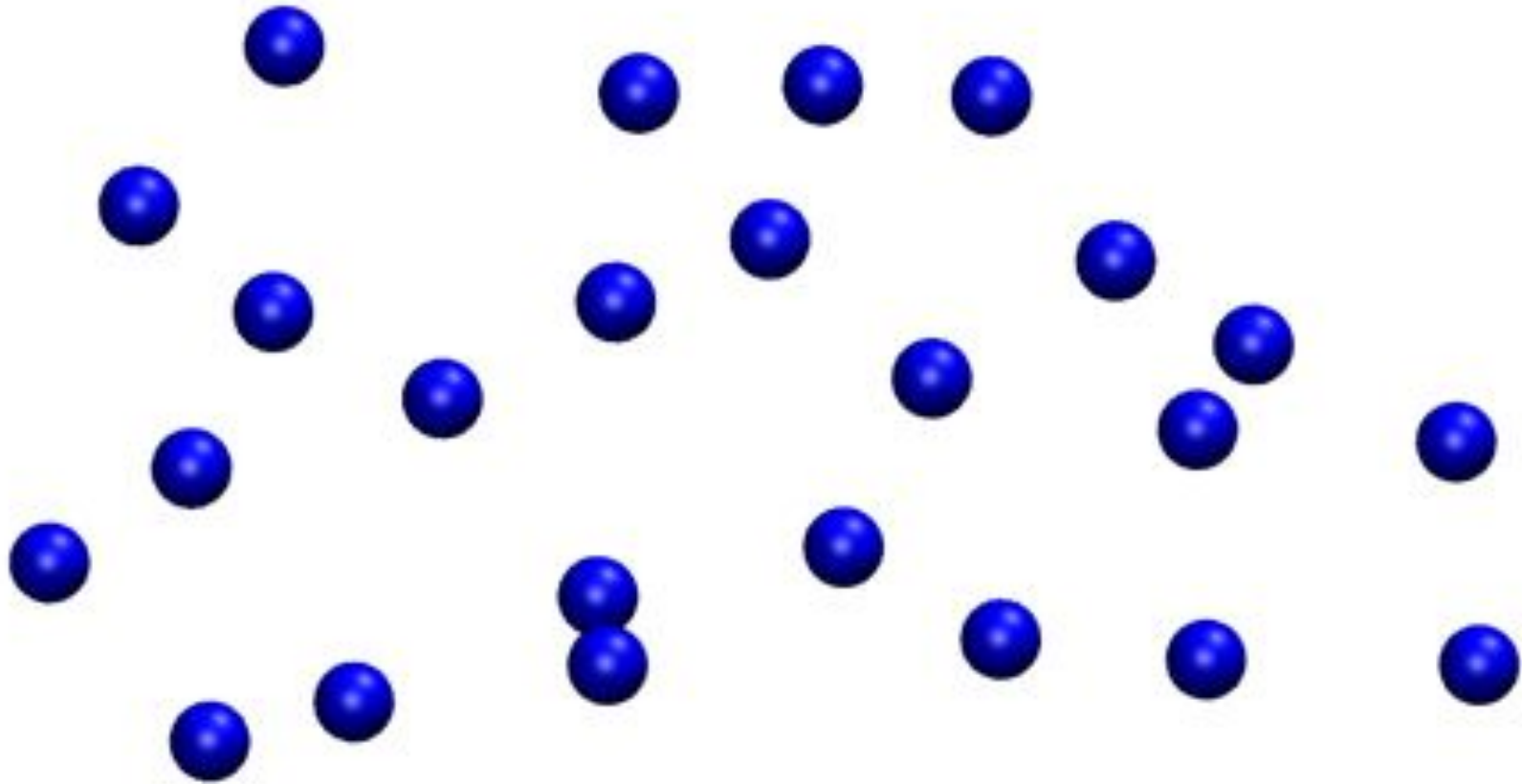
Charging tRNA through allosteric signaling



Overall Charging Reaction

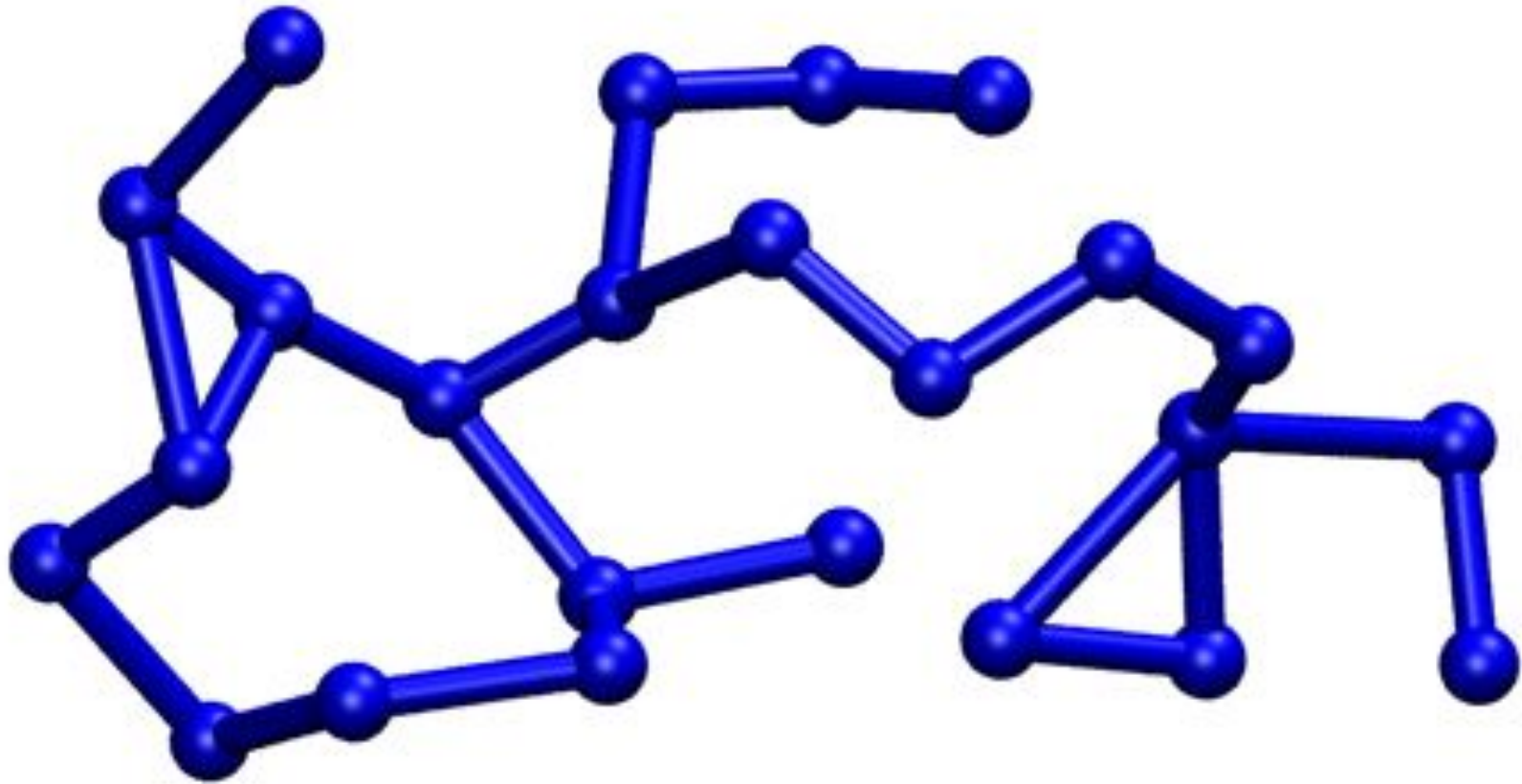


How to Construct a Network?



Nodes - defined at C_{α} (protein) and P (nucleotide) atoms

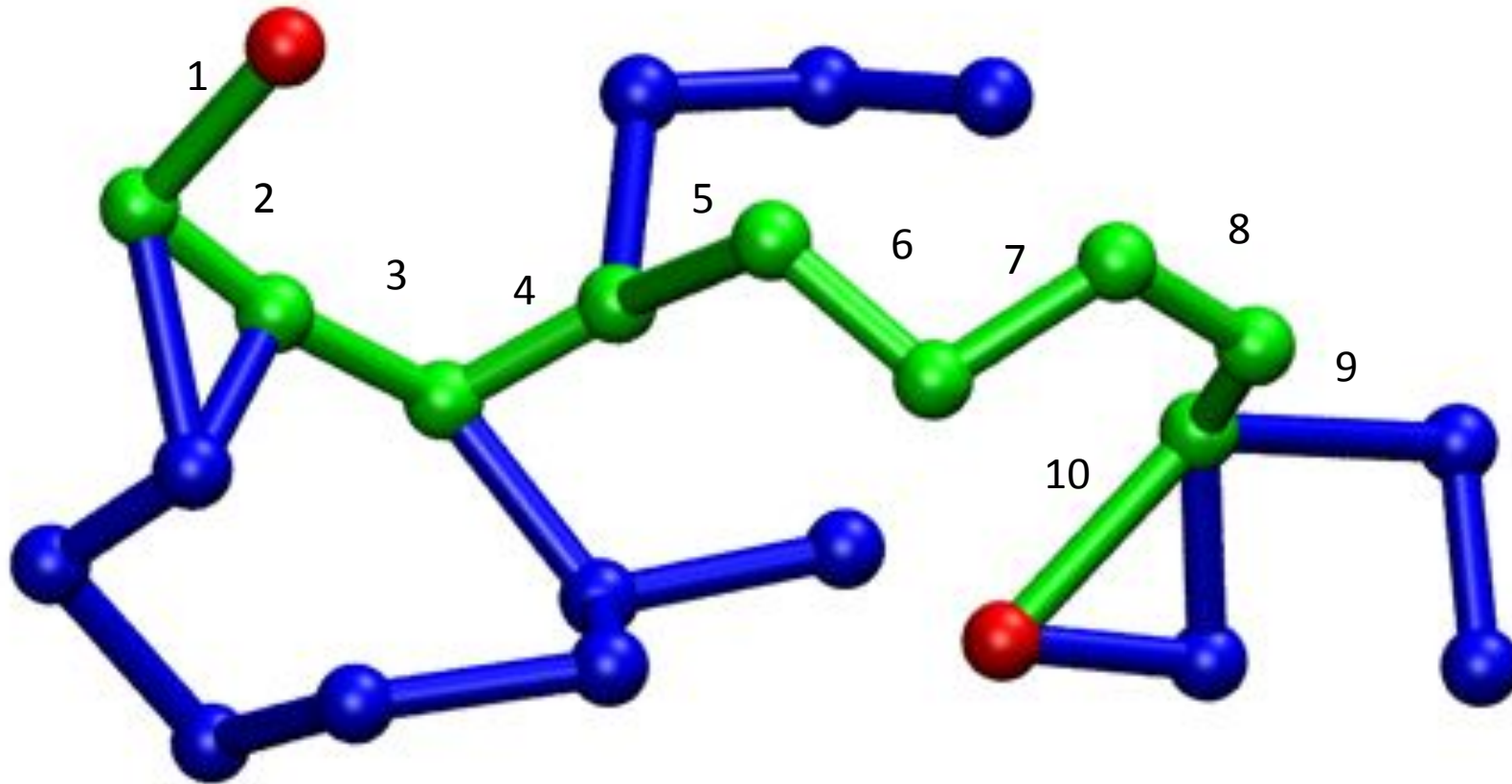
How to Construct a Network?



Edges - connect nodes that are within a contact distance threshold for more than 75% of an MD trajectory

Communication between Identity Elements and Site of Chemistry

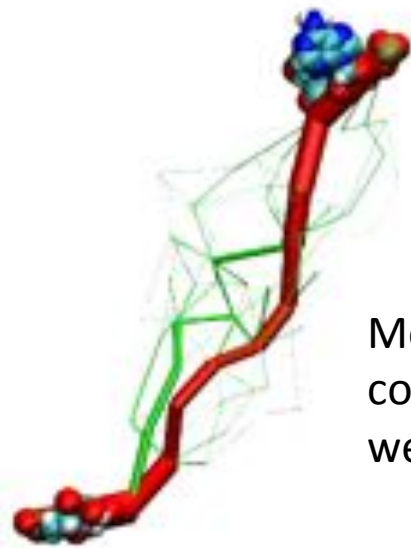
Different Paths can have Different Lengths



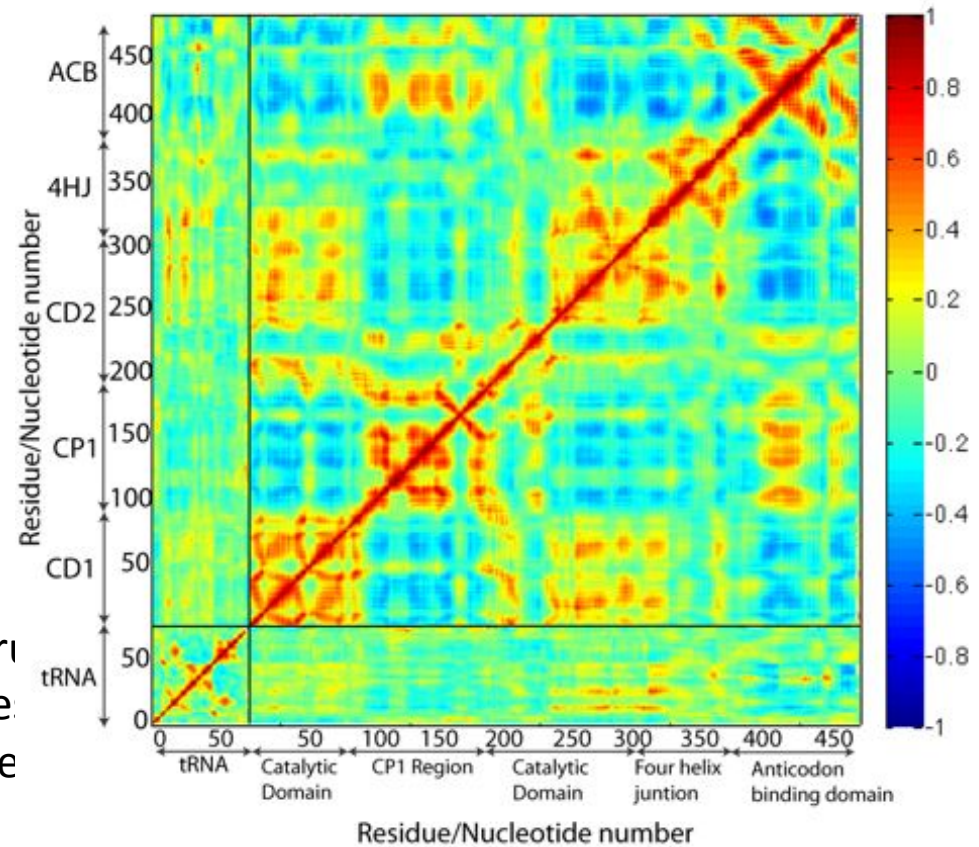
Path length = 10 (*unweighted*)

Information transfer? Weight contacts/links by correlations !

Correlations (C_{ij}) define signaling pathways in GluRS:tRNA

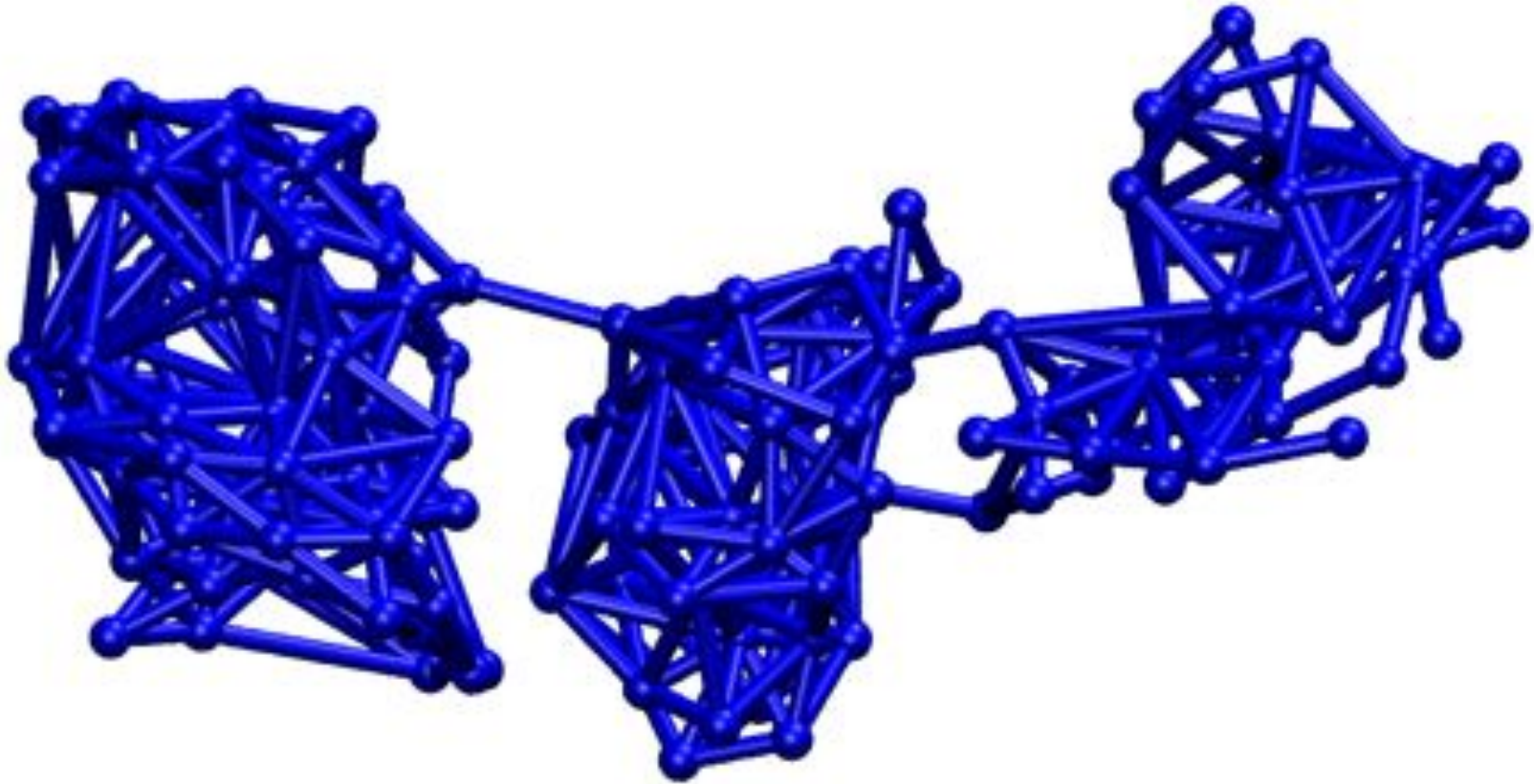


Modular structure
community
weighted network

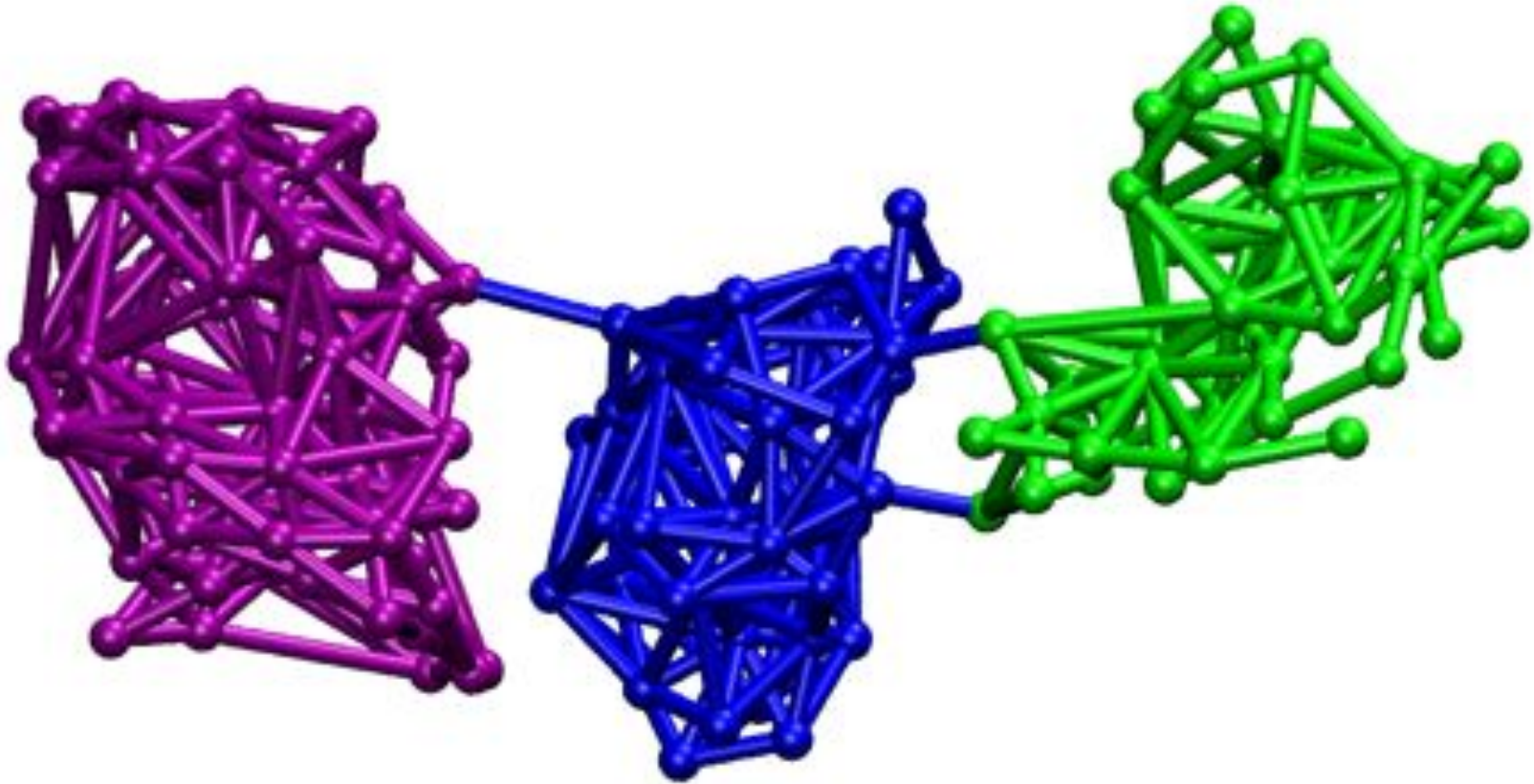


- MD simulations run with NAMD
- NTP ensemble
- Neutralized with Mg^{2+} and K^+
- C_{ij} values calculated over a 16-ns window

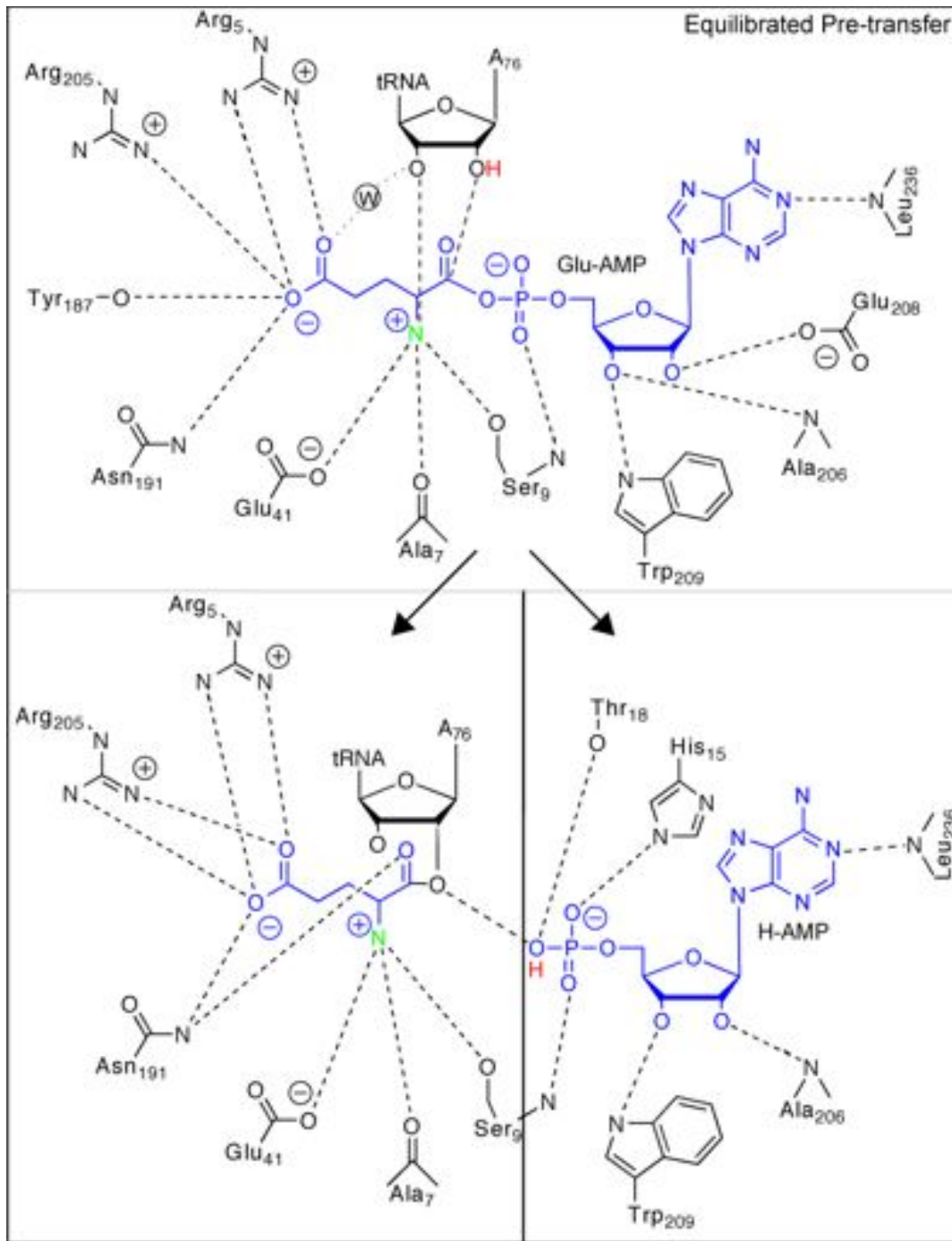
Nodes Cluster Together in Modules called
Communities



Nodes Cluster Together in Modules called Communities



Communities are subnetworks with many intracommunity edges but few intercommunity edges.

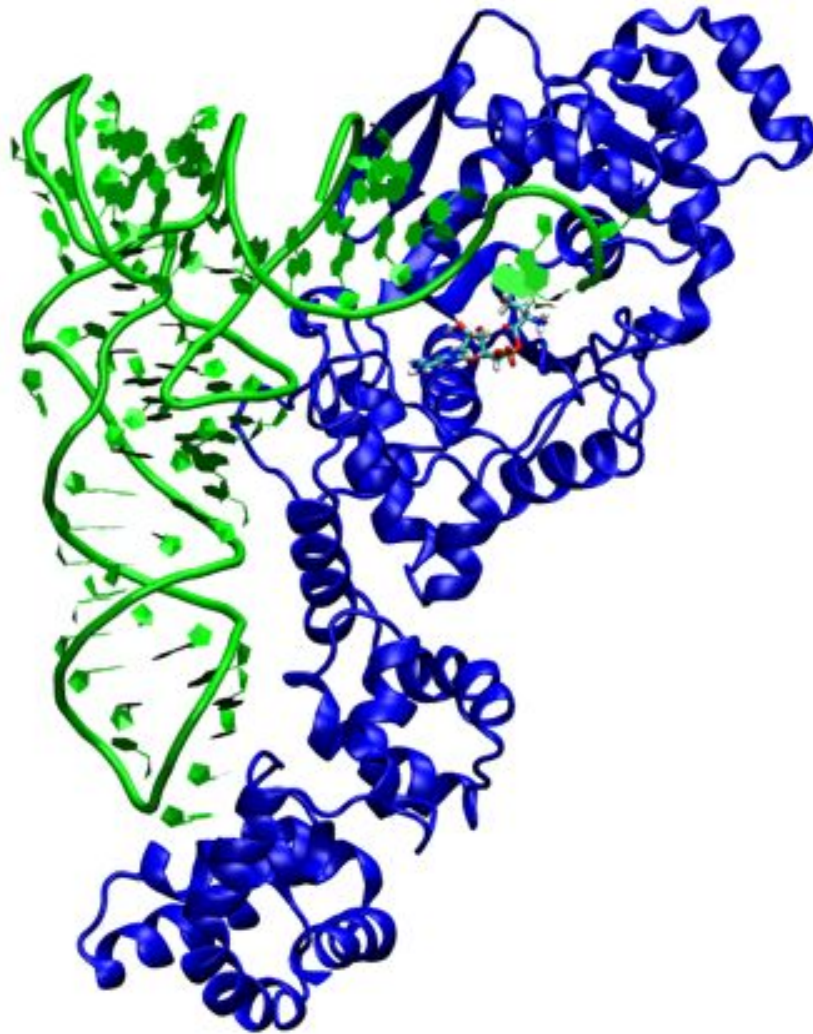


Reaction Mechanism for the Transfer of Glu to tRNA^{Glu}

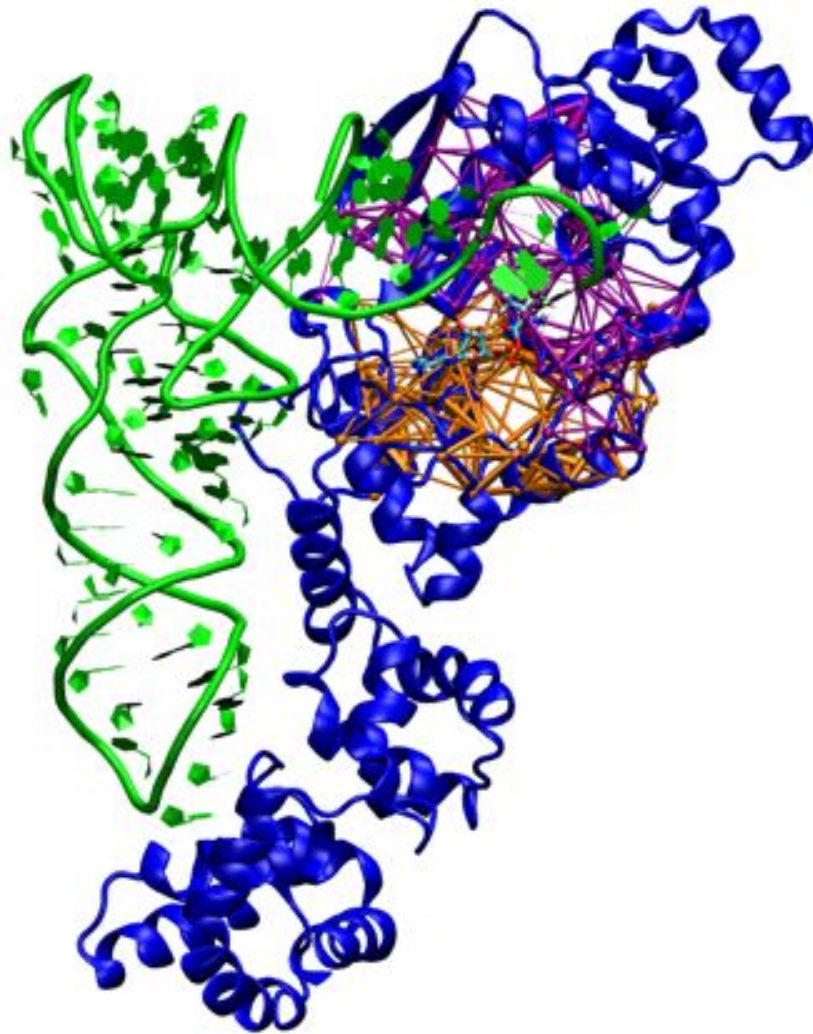
Perona JJ, Rould MA, Steitz TA
Biochemistry 1993

Black A, Eargle J, Sethi A,
Luthey-Schulten Z. *JMB* 2010
100s ns MD simulations

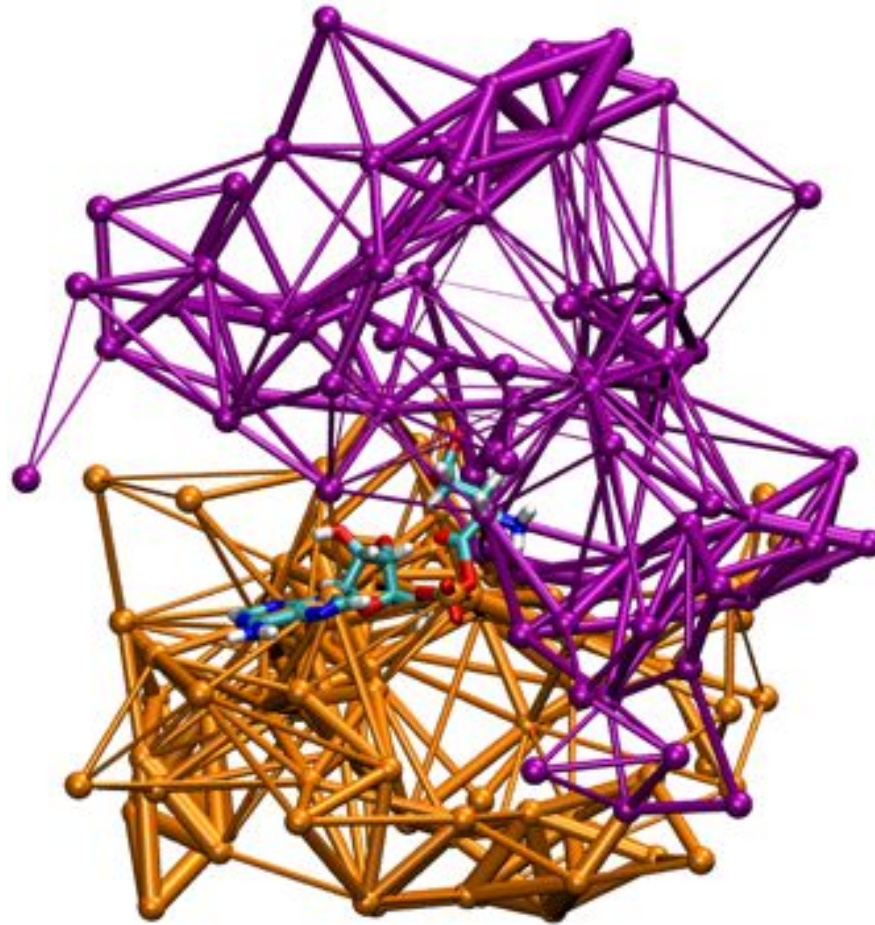
Community Structure Reveals Function in GluRS



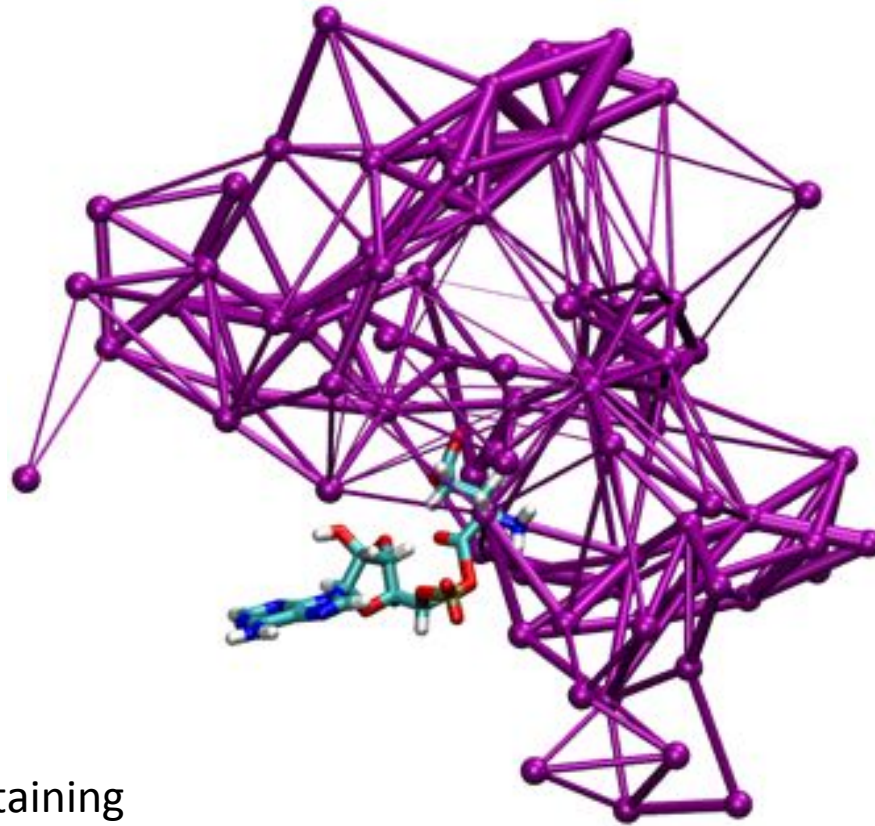
Community Structure Reveals Function in GluRS



Community Structure Reveals Function in GluRS



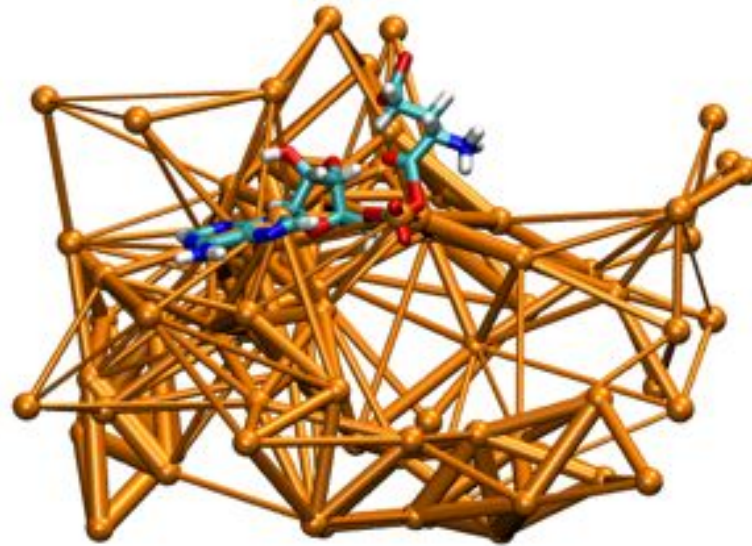
Community Structure Reveals Function in GluRS



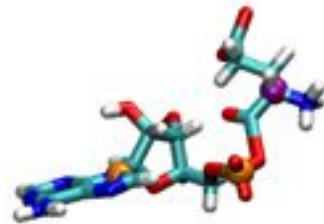
community containing
amino acid moiety

Community Structure Reveals Function in GluRS

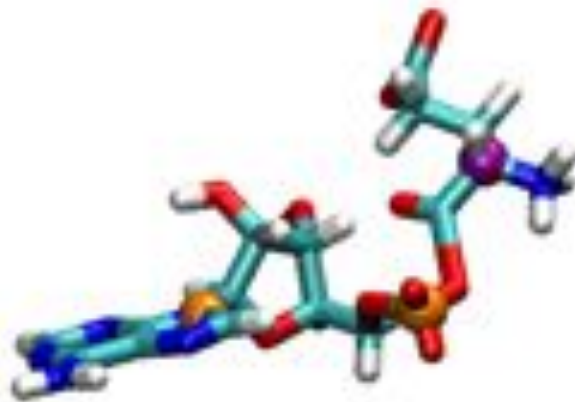
community containing
AMP moiety



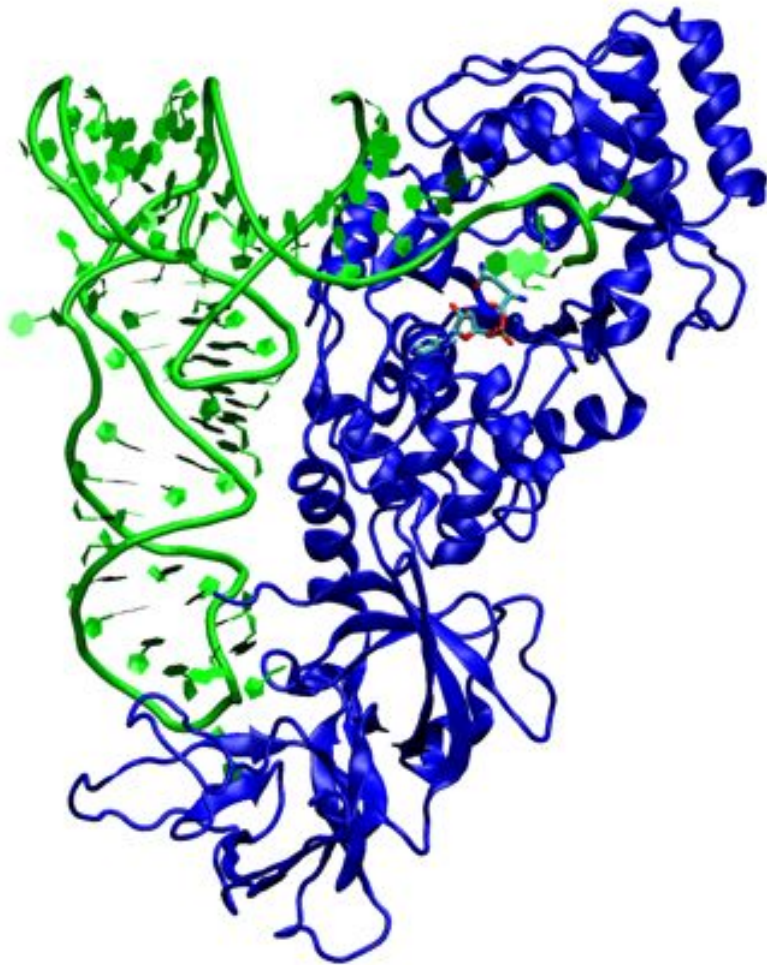
Community Structure Reveals Function in GluRS



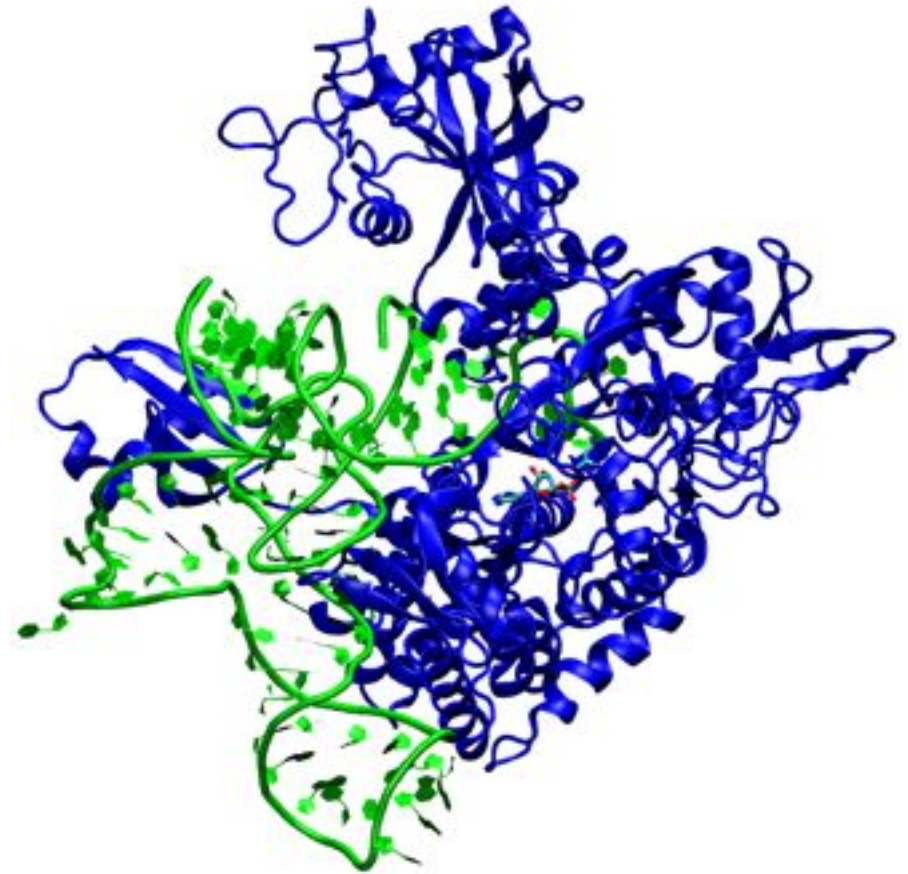
Community Structure Reveals Function in GluRS



Similar Ligand Separation in GlnRS and LeuRS

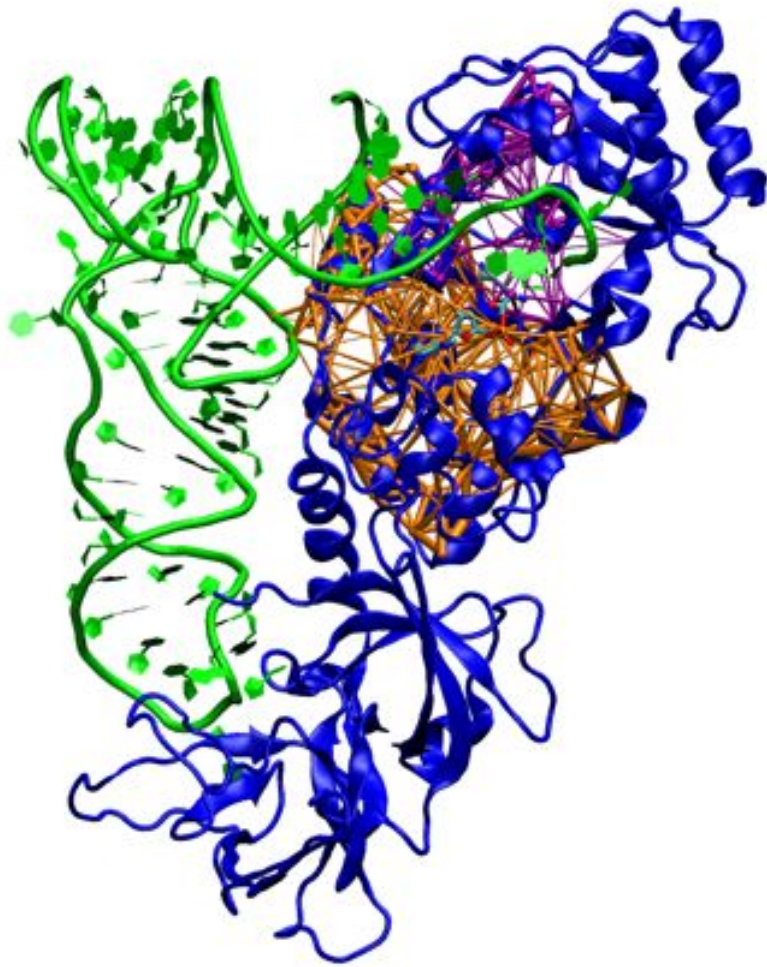


GlnRS



LeuRS

Similar Ligand Separation in GlnRS and LeuRS

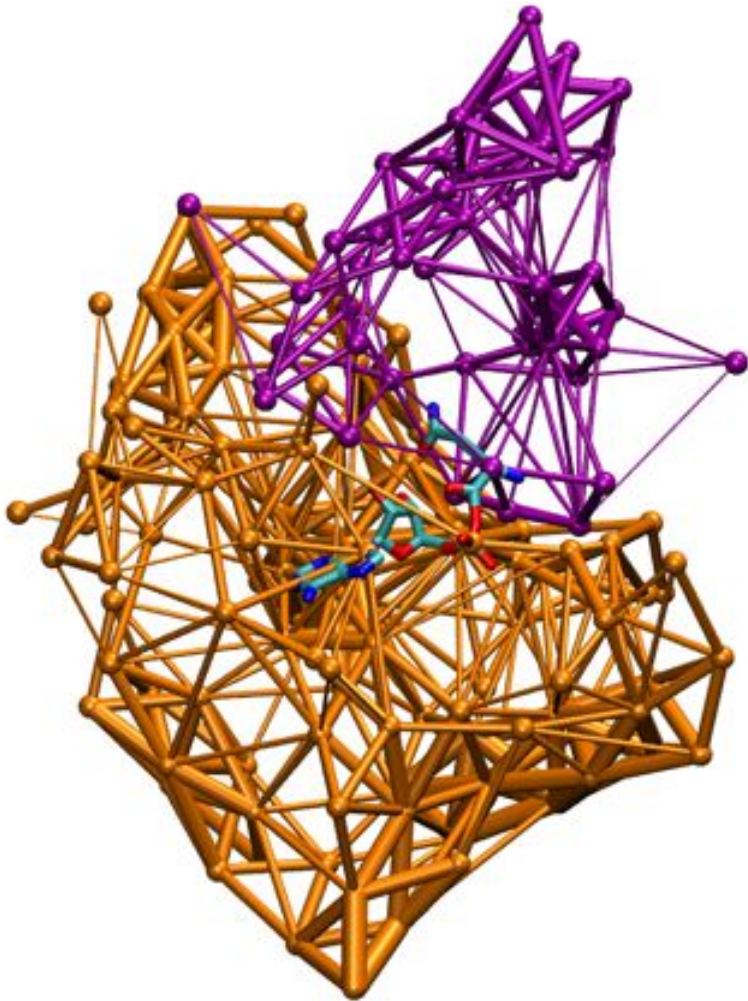


GlnRS

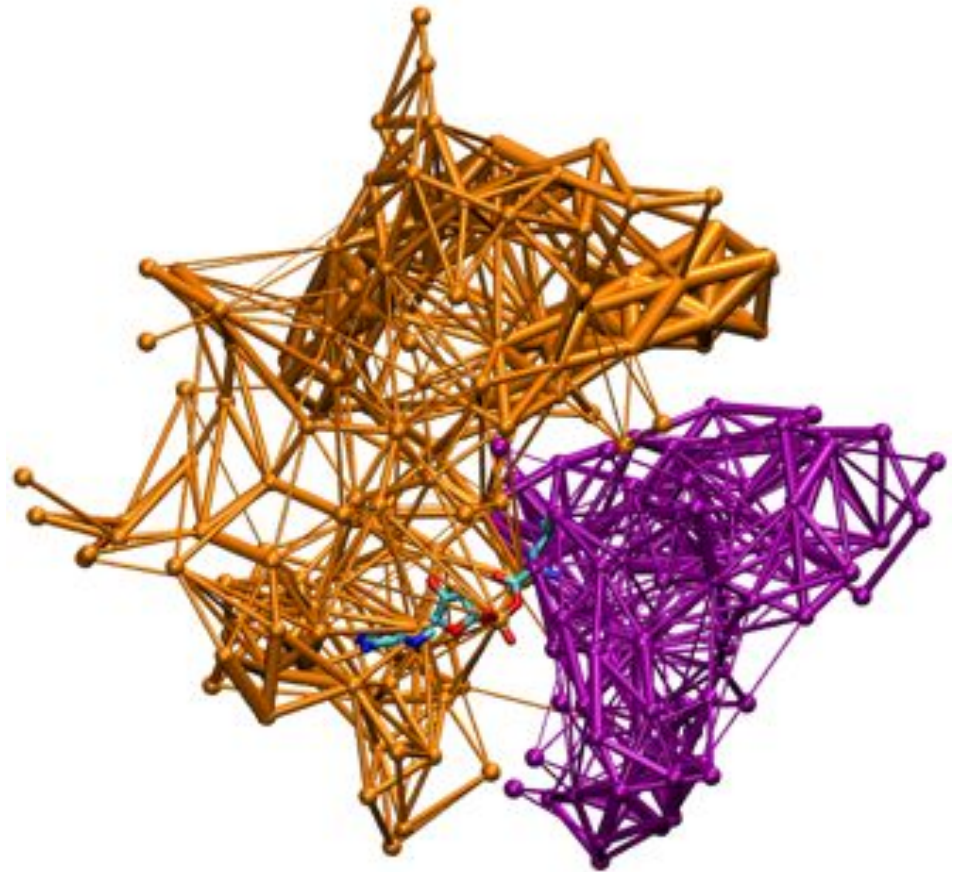


LeuRS

Similar Ligand Separation in GlnRS and LeuRS

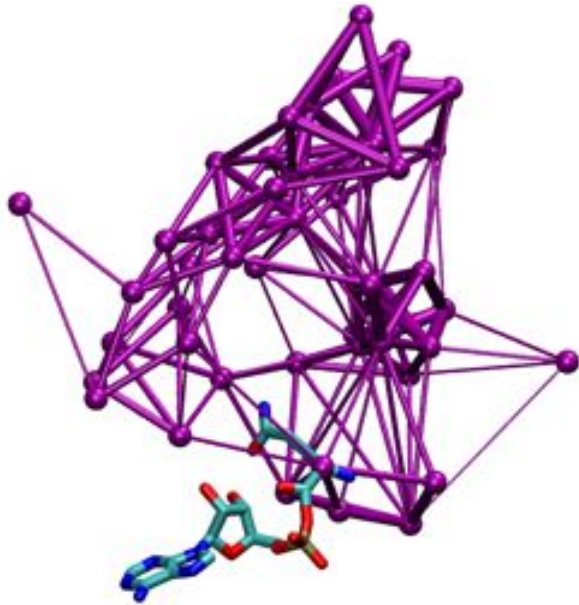


GlnRS



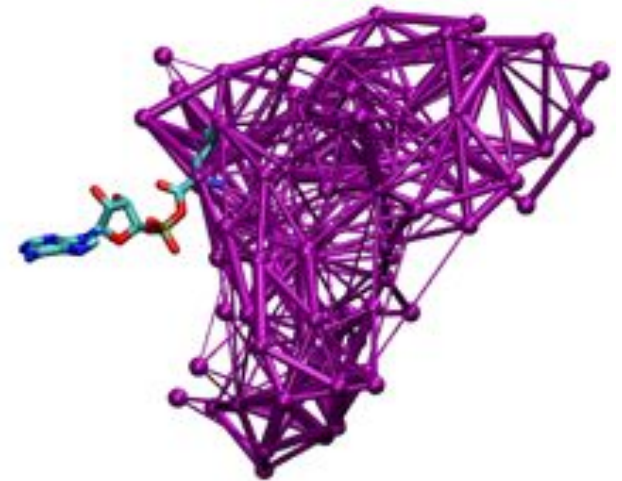
LeuRS

Similar Ligand Separation in GlnRS and LeuRS



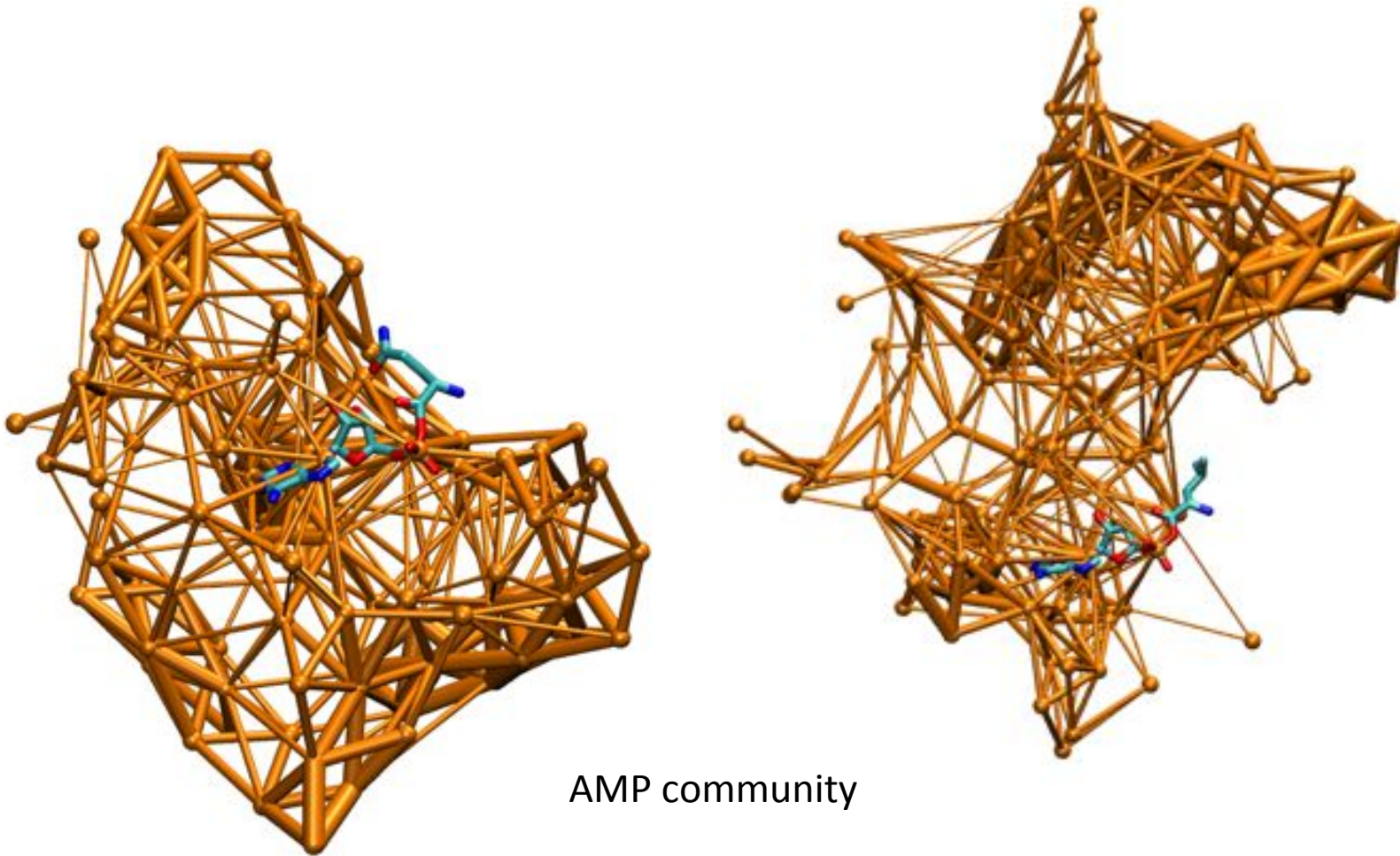
Amino acid community

GlnRS



LeuRS

Similar Ligand Separation in GlnRS and LeuRS

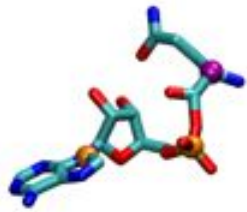


GlnRS

LeuRS

AMP community

Similar Ligand Separation in GlnRS and LeuRS

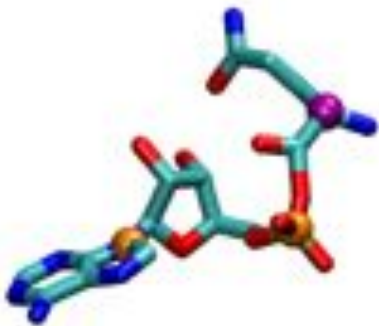


GlnRS

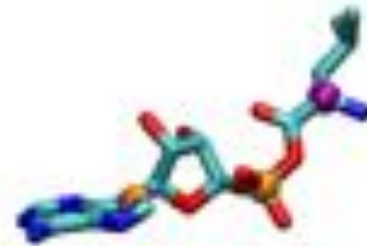


LeuRS

Similar Ligand Separation in GlnRS and LeuRS

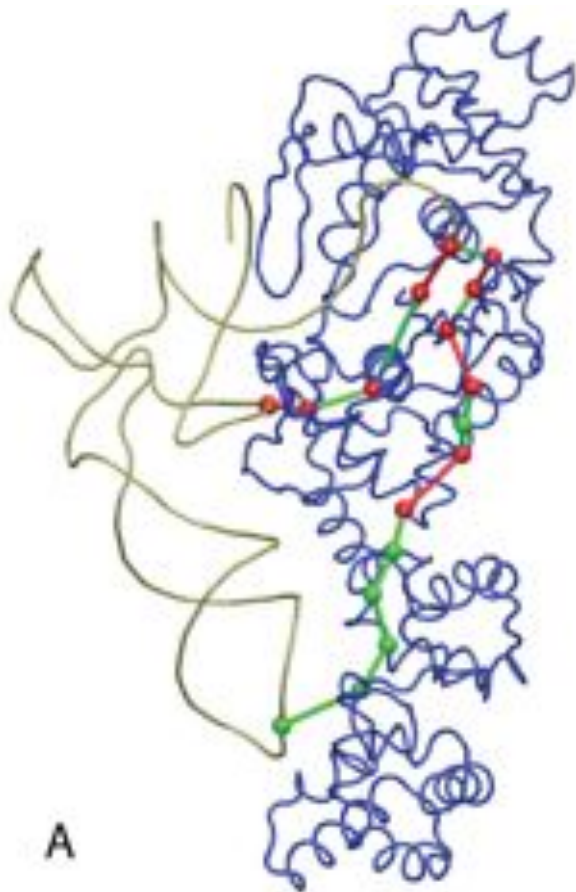


GlnRS



LeuRS

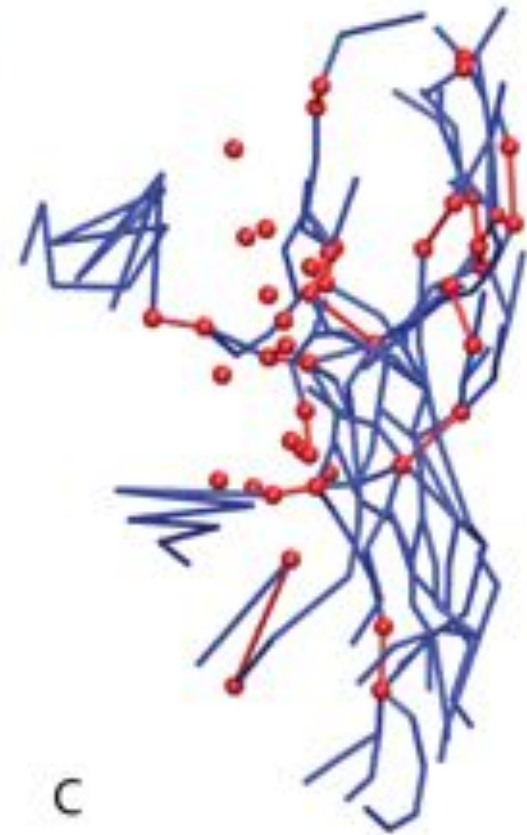
Dynamical Networks, Conservation, and Betweenness



Optimal signal pathways:
U13, U35 to A76



Critical(conserved) nodes
connecting communities



Betweenness routes - highest
density pair optimal paths