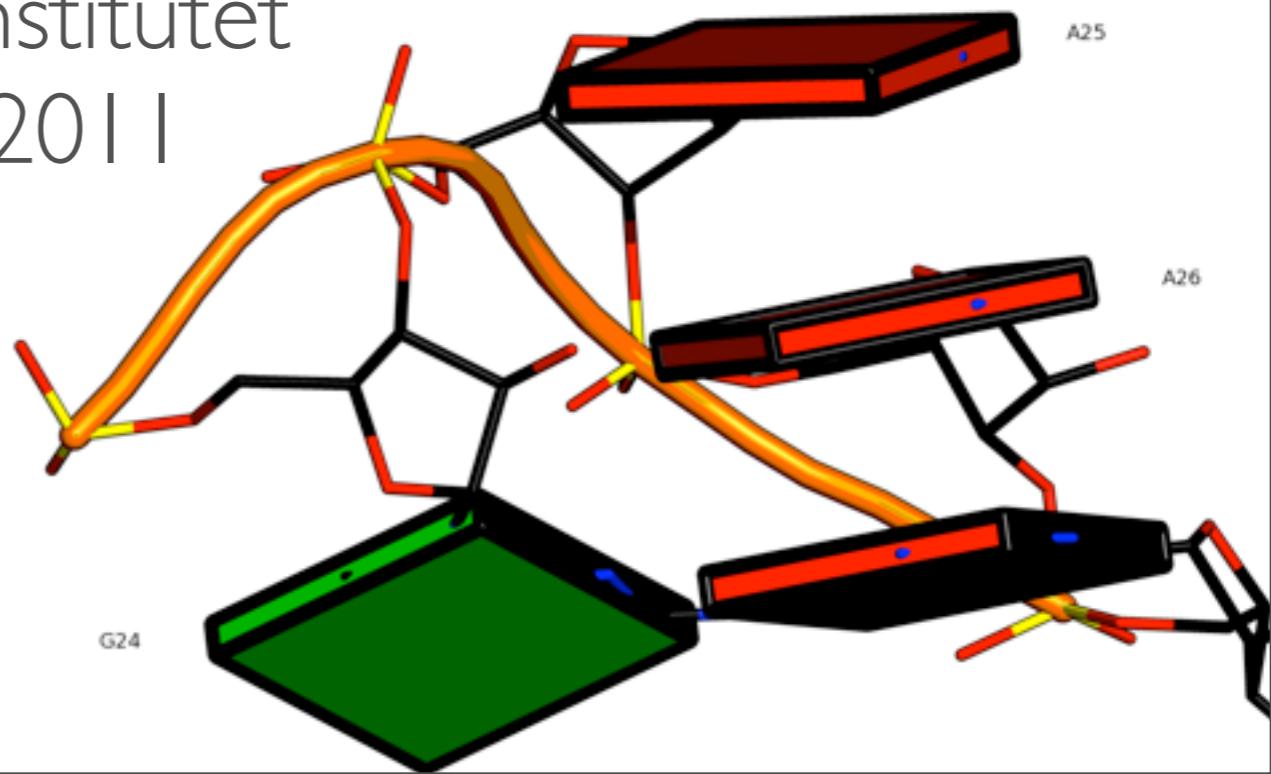


THE RIGID BODY MODEL FOR NUCLEIC ACIDS

Mauricio Esguerra
Karolinska Institutet
Abril 29, 2011



Karta Flygfoto Hybrid Sjökort Utsikt Gatuvy





Vad söker du?

produkt, tjänst, företag, person, nummer

Var?

område, adress, plats, ort

Kartsök

Företag

Personer

Kartor

Vägbeskrivning

Begagnat

WebT

Skriv ut

Länk till kartan





Thursday, April 28, 2011

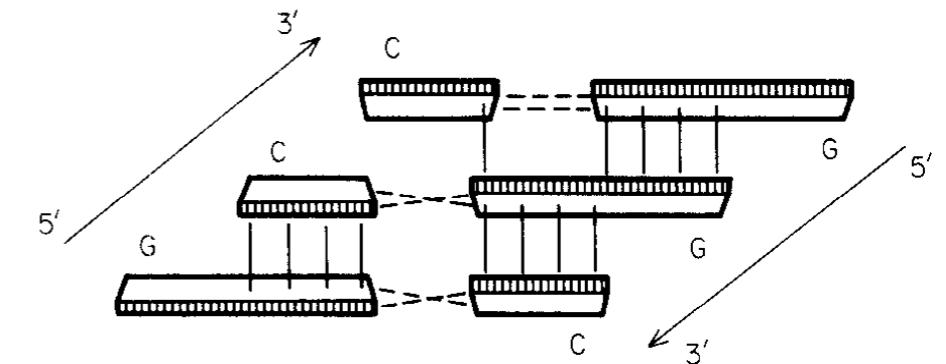
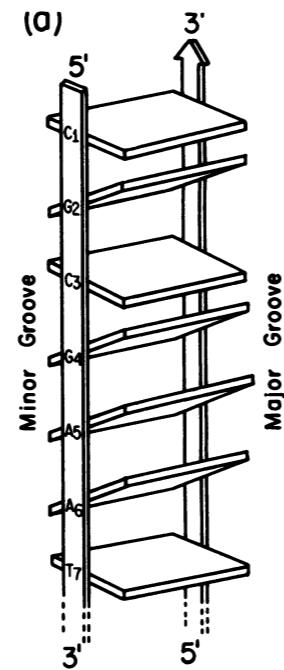
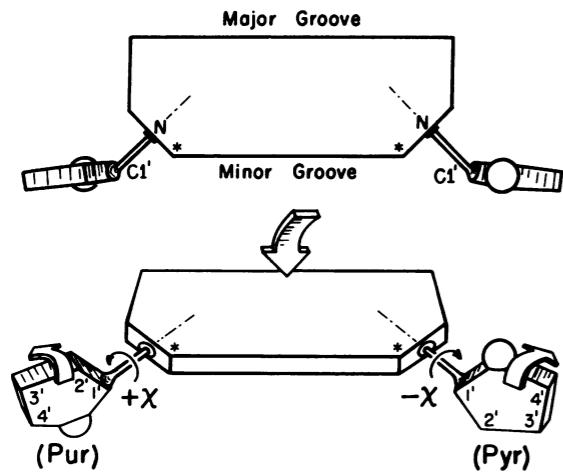
HISTORICAL OVERVIEW

- 1953 Watson-Crick.
- 1980's block models are popular. Dickerson-Drew dodecamer (1981). Calladine-Drew A to B conformational change seen from the base perspective.
- 1988 Cambridge accord for base-pair and bp step parameters.
- 1999 Tsukuba / 2001 JMB Standard Reference Frame.
- 2003 13th Albany Conversation Standard Method.
3DNAVI
- 2008 3NAV2
- 2009 Curves+



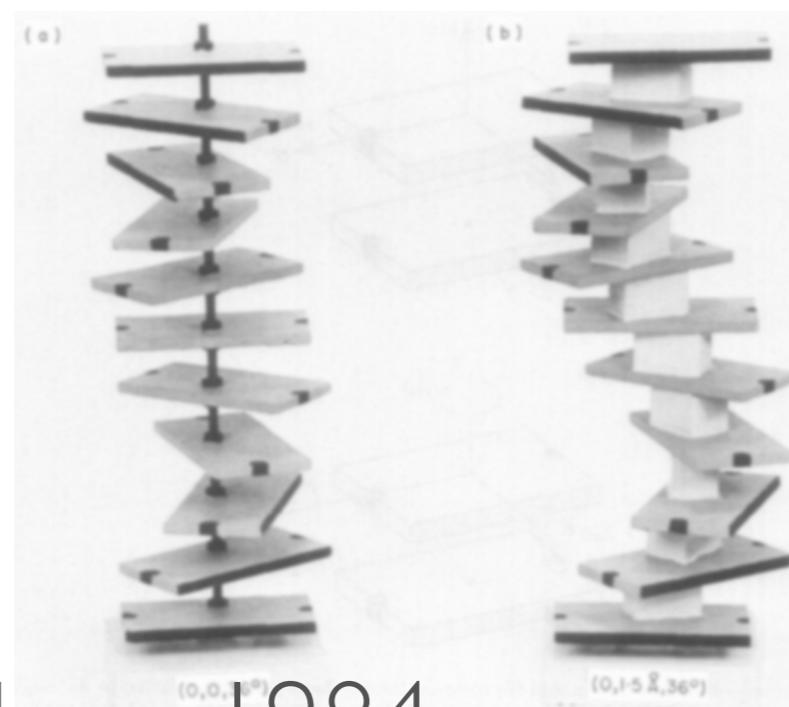
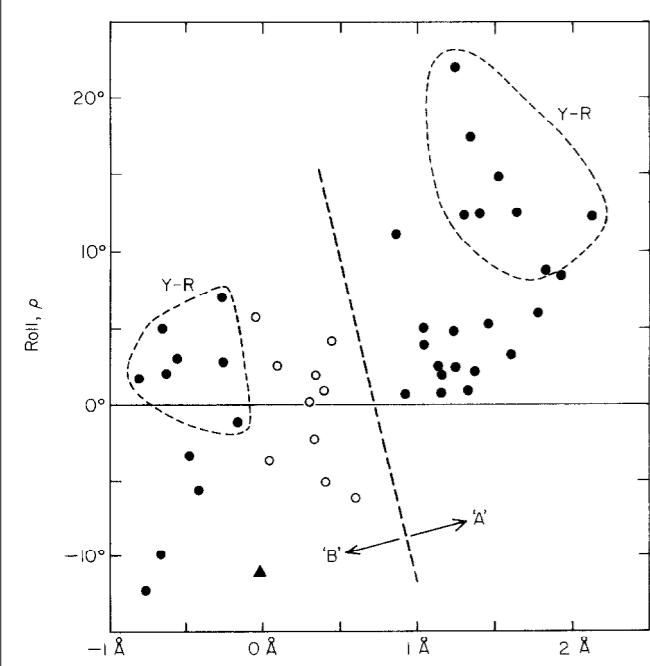
This figure is purely diagrammatic. The two ribbons symbolize the two phosphate-sugar chains, and the horizontal rods the pairs of bases holding the chains together. The vertical line marks the fibre axis

THESE ARE THE EIGHTIES FOR NUCLEIC ACIDS

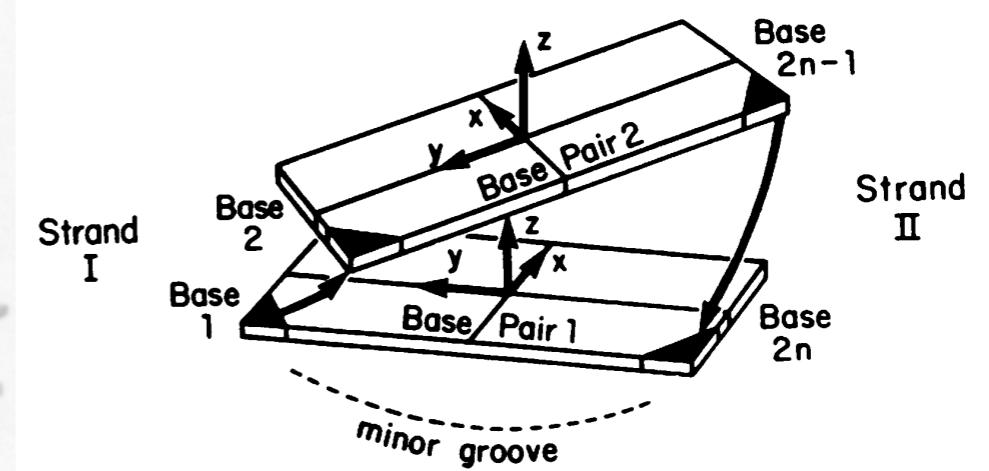


calladine-drew 1986

dickerson-drew 1981



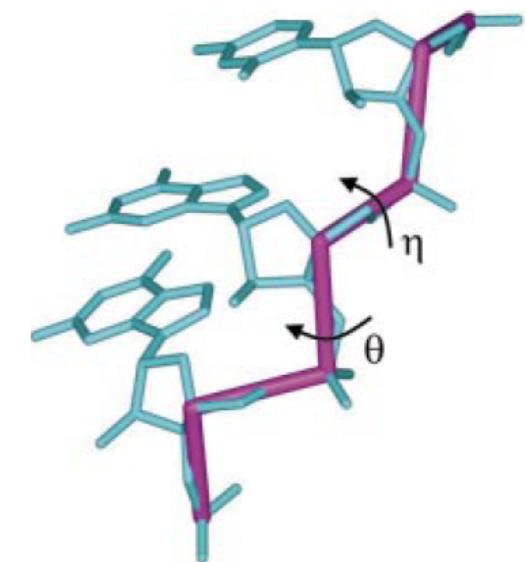
calladine-drew 1984



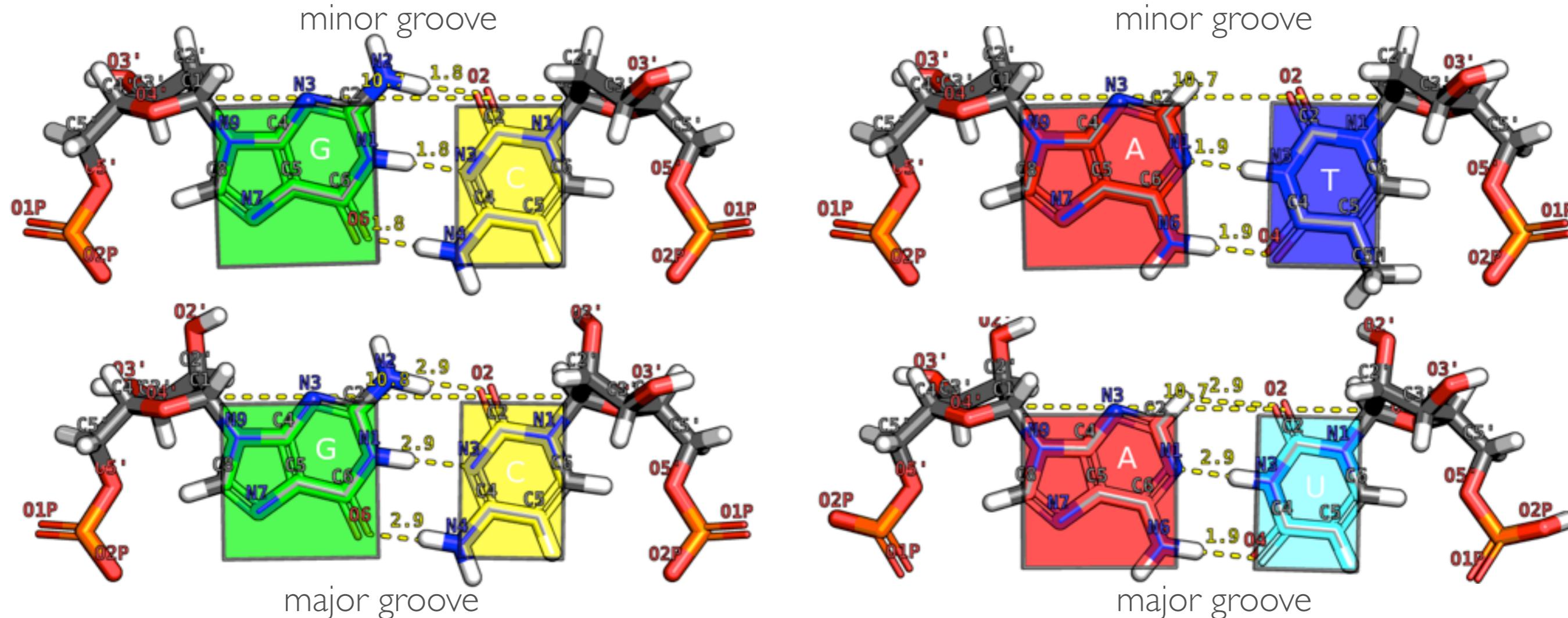
dickerson et al. 1989

ALTERNATE DESCRIPTIONS OF MOLECULAR STRUCTURE

- All-atom
 - classic mechanics
 - quantum mechanics
- Coarse-Grained
 - reduced set of atoms, e.g. C α in proteins.
 - pseudo-bond/angles
 - **rigid-bodies**, e.g. “just like lego blocks”



NDB/PDB COLOR CONVENTION

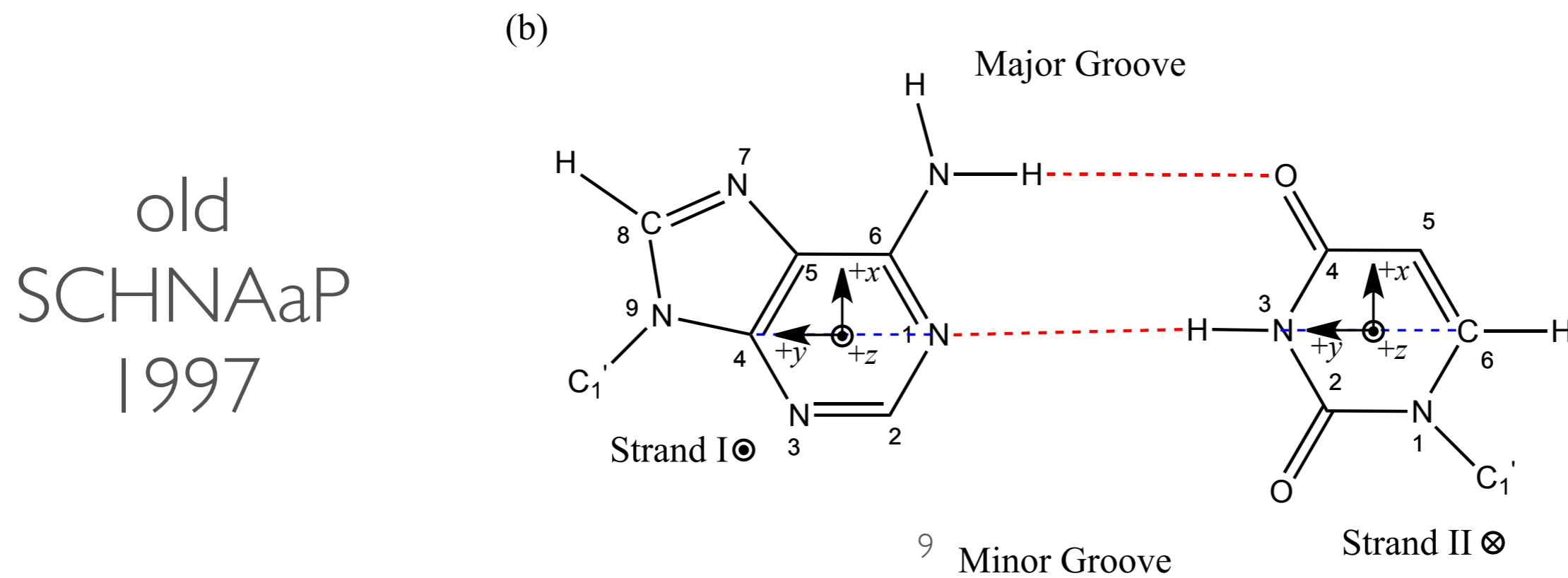
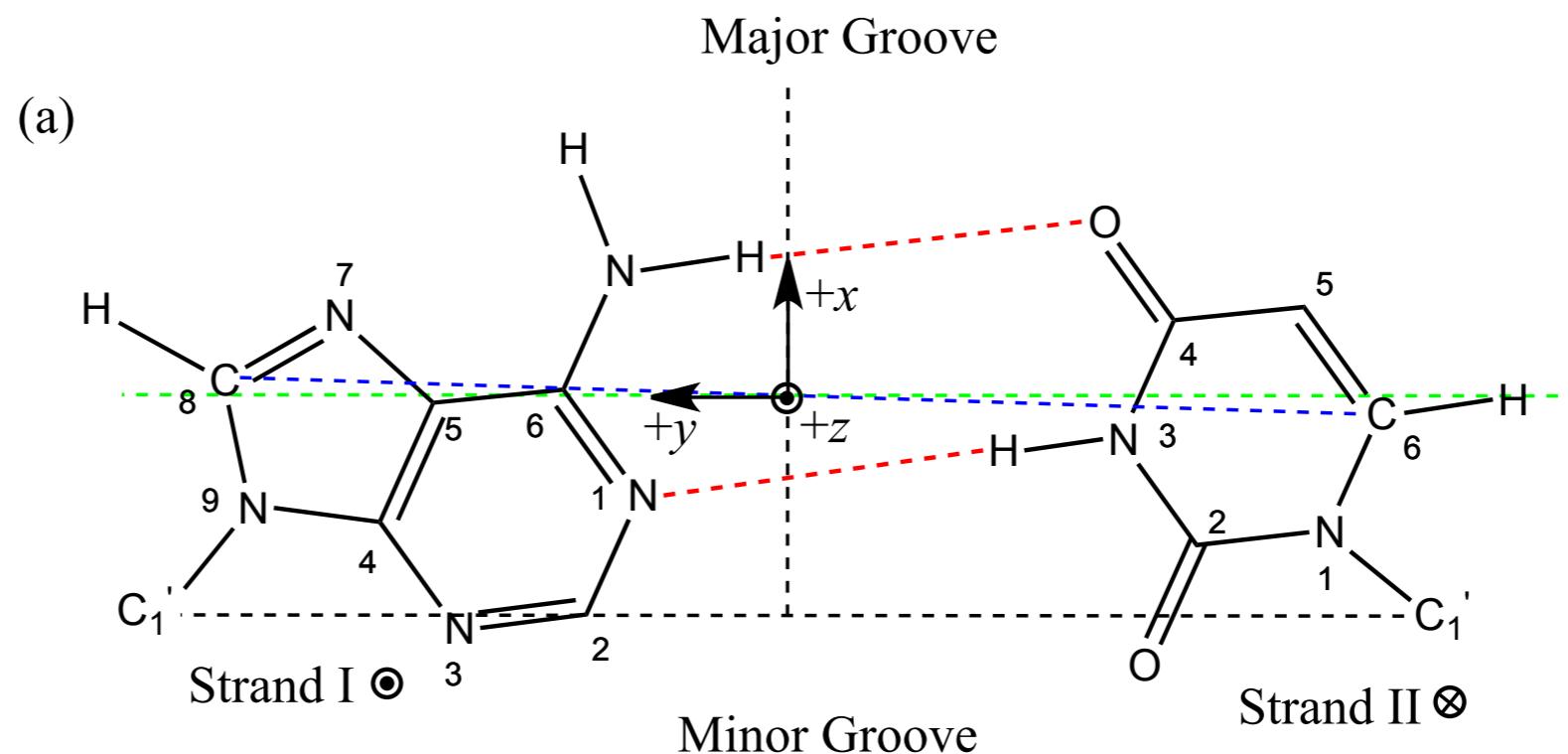


Purines aka **R** = Guanine (green) and Adenine (red)

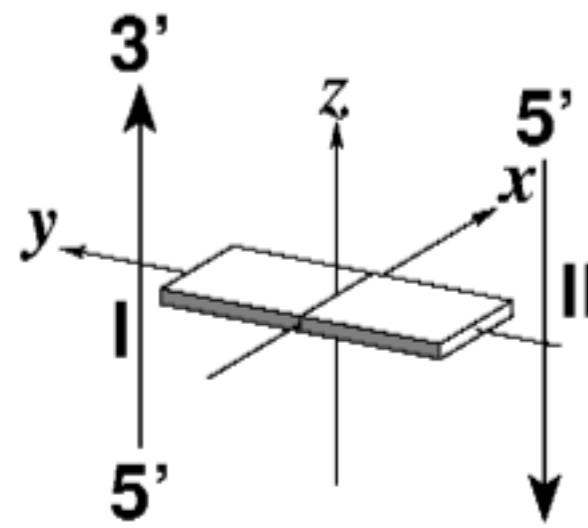
Pyrimidines aka **Y** = Cytosine (yellow), Thymine (blue) and Uracil (cyan)

STANDARD REFERENCE FRAME

new
3DNA,
Curves+
 | 1999-2001 |

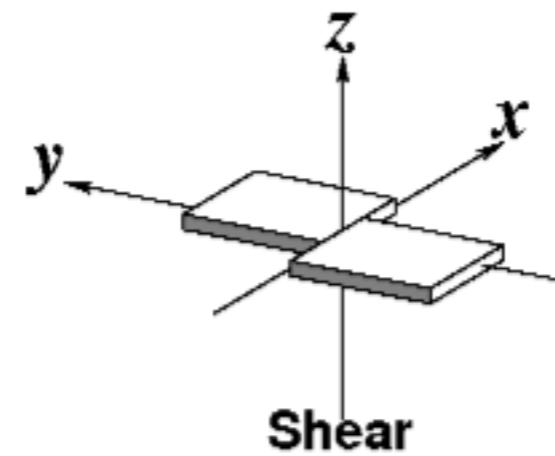


CALLADINE-DREW RIGID-BLOCK MODEL

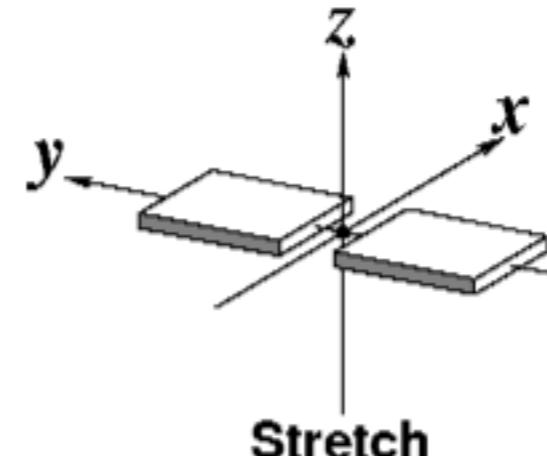


Base-Pair Parameters

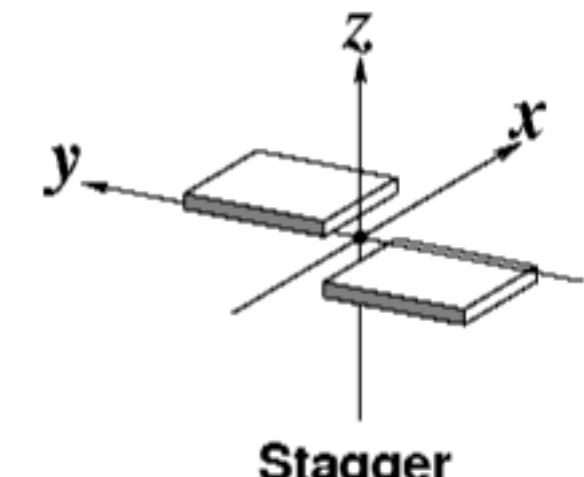
translation



Shear

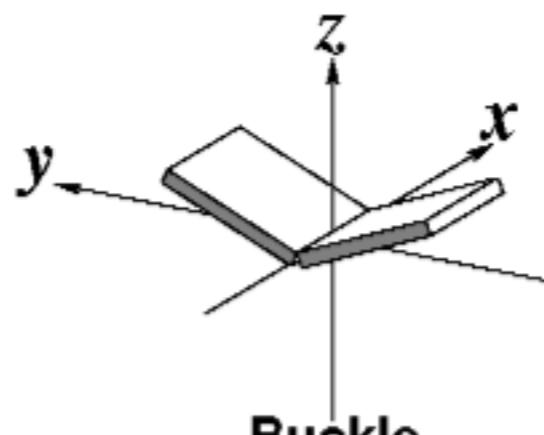


Stretch

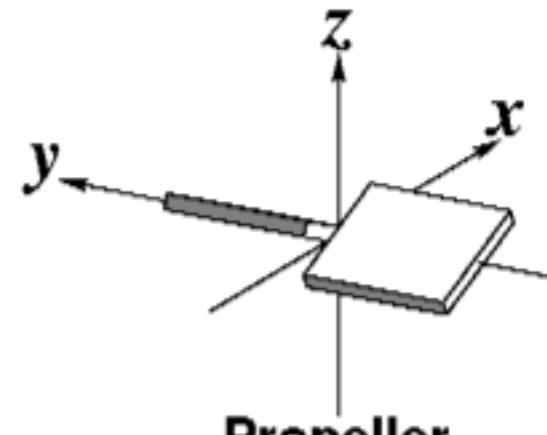


Stagger

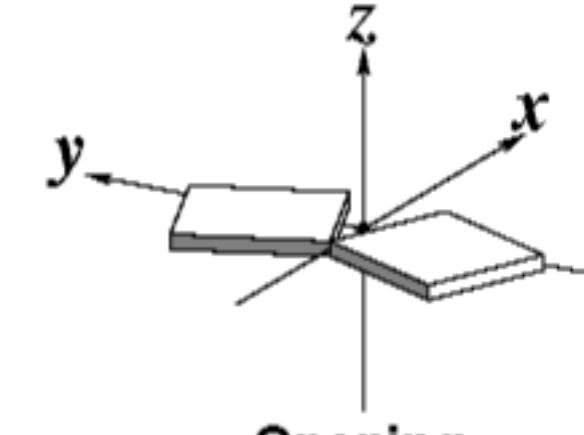
rotation



Buckle



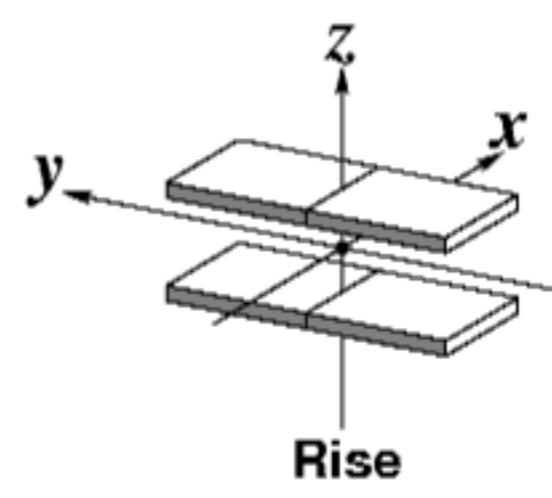
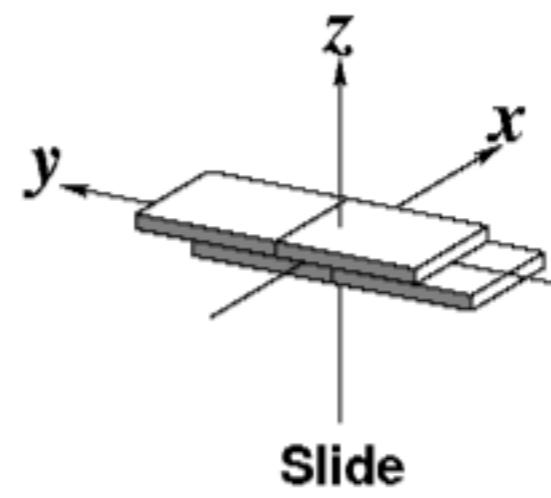
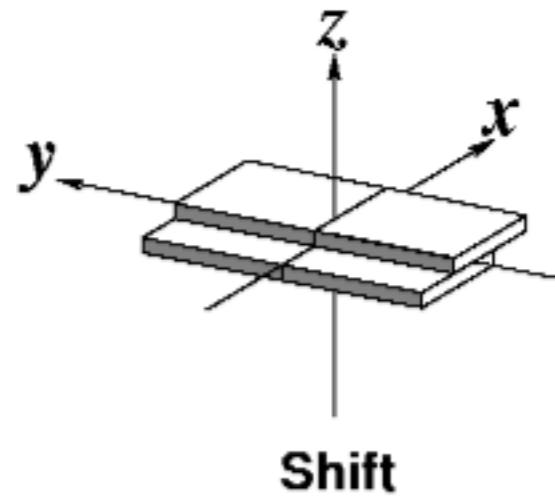
Propeller



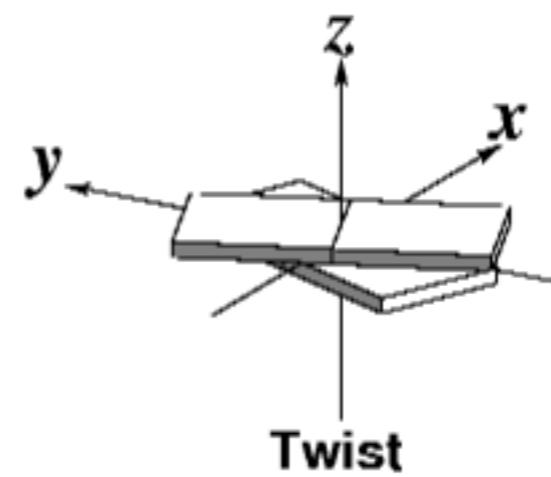
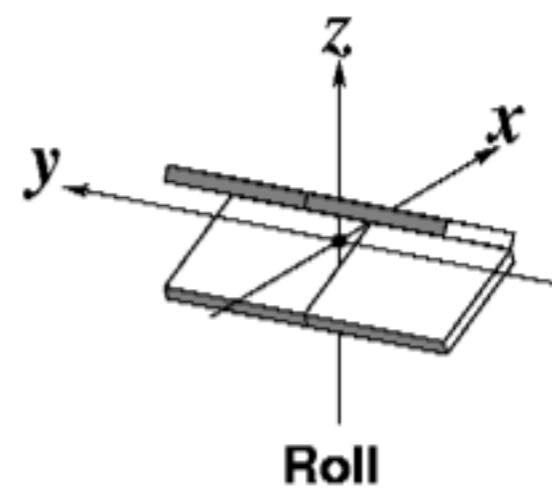
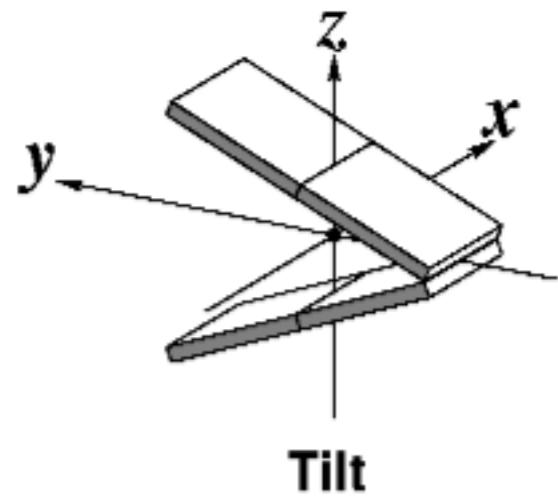
Opening

CALLADINE-DREW RIGID-BLOCK MODEL

Base-Pair-Step Parameters



translation



rotation

PROGRAMS TO COMPUTE RIGID-BODY PARAMETERS. BASE-CENTERED FORMALISM

NEW

- **3DNA** (Xiang-Jun Lu @ Columbia, Bussemaker lab.)
 - <http://w3dna.rutgers.edu>
 - <http://rutchem.rutgers.edu/~xiangjun/3DNA>
 - 3dnaV2, UNIX preferred (linux, OS-X, freebsd, cygwin “yikes!”)
- curves+ (Richard Lavery @ Universite d' Lyon)

OLD

- FREEHELIX, RNA, SCHNAAp, SCHNArP, compDNA, NUPARM

WHAT'S A BASE-PAIR IN 3DNA?

look at misc_3dna.par

- The distance between the origins of the two bases (as defined by their standard reference frames) must be less than certain limit (15.0 Å by default) - otherwise, they would be too far away to be called a pair.
- The vertical separation (i.e., stagger) between the two bases must be less than certain limit (2.5 Å by default) - otherwise, they would be stacking instead of pairing.
- The angle between the two base z-axes (i.e., their normal vectors) is less than a cut-off (65.0° by default).
- There is at least one pair of nitrogen/oxygen base atoms that are within a H-bonding cut off distance (4.0 Å by default).

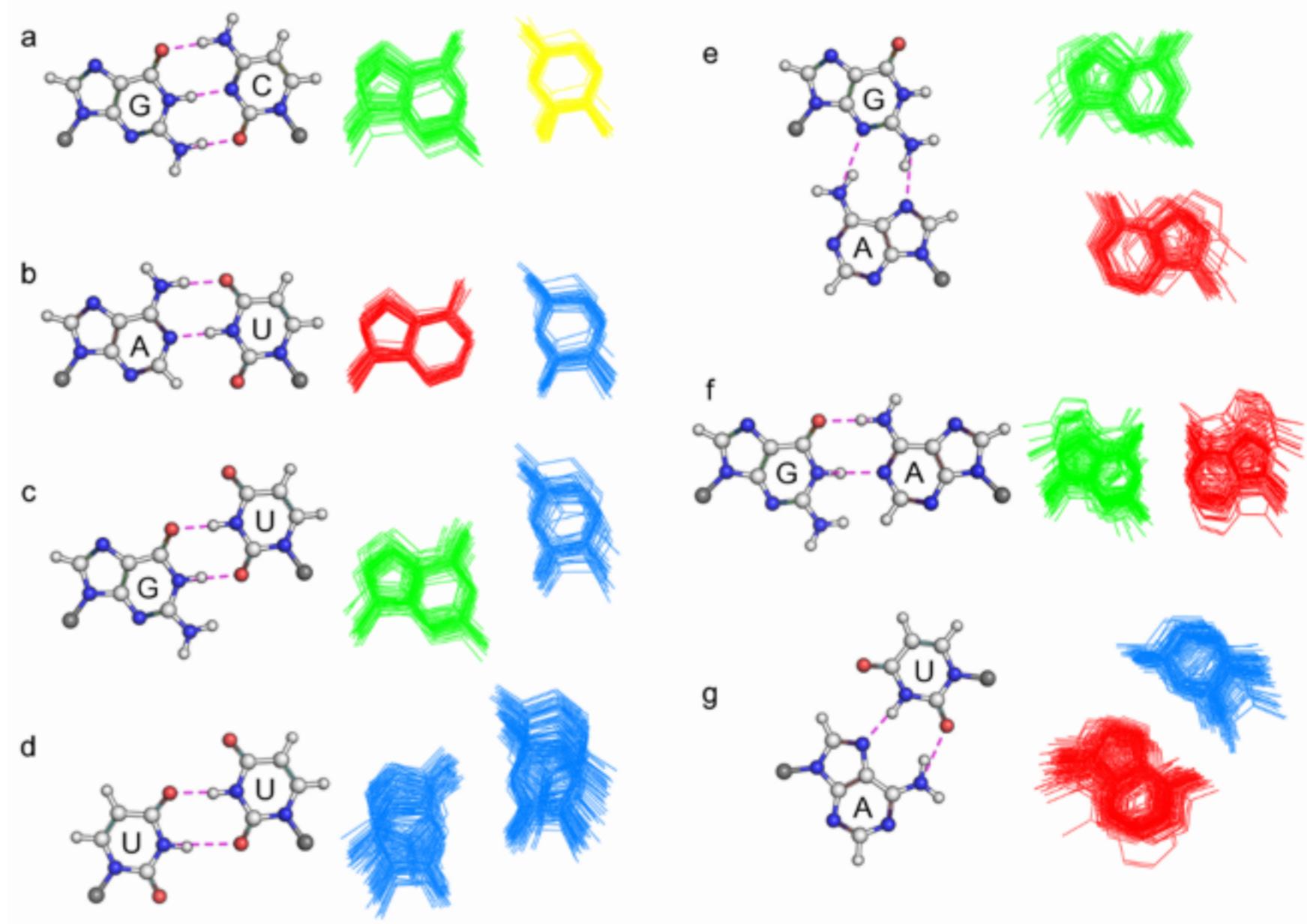
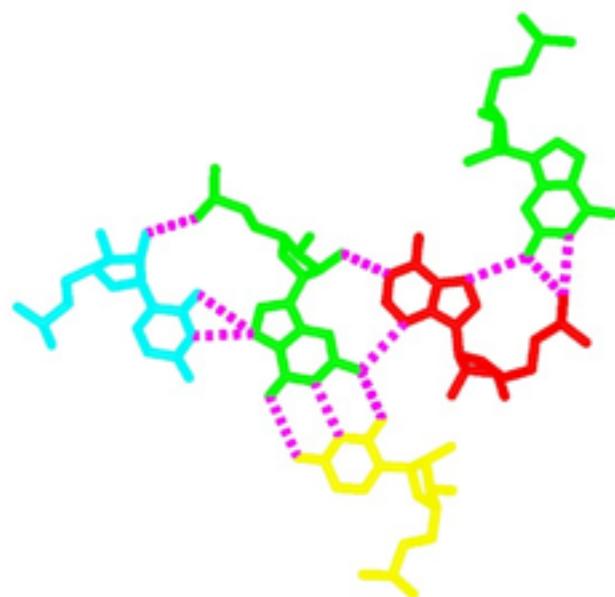
BASE-PAIR DATABASES

- <http://bps.rutgers.edu> for RNA
- <http://3dnascapes.rutgers.edu> for DNA

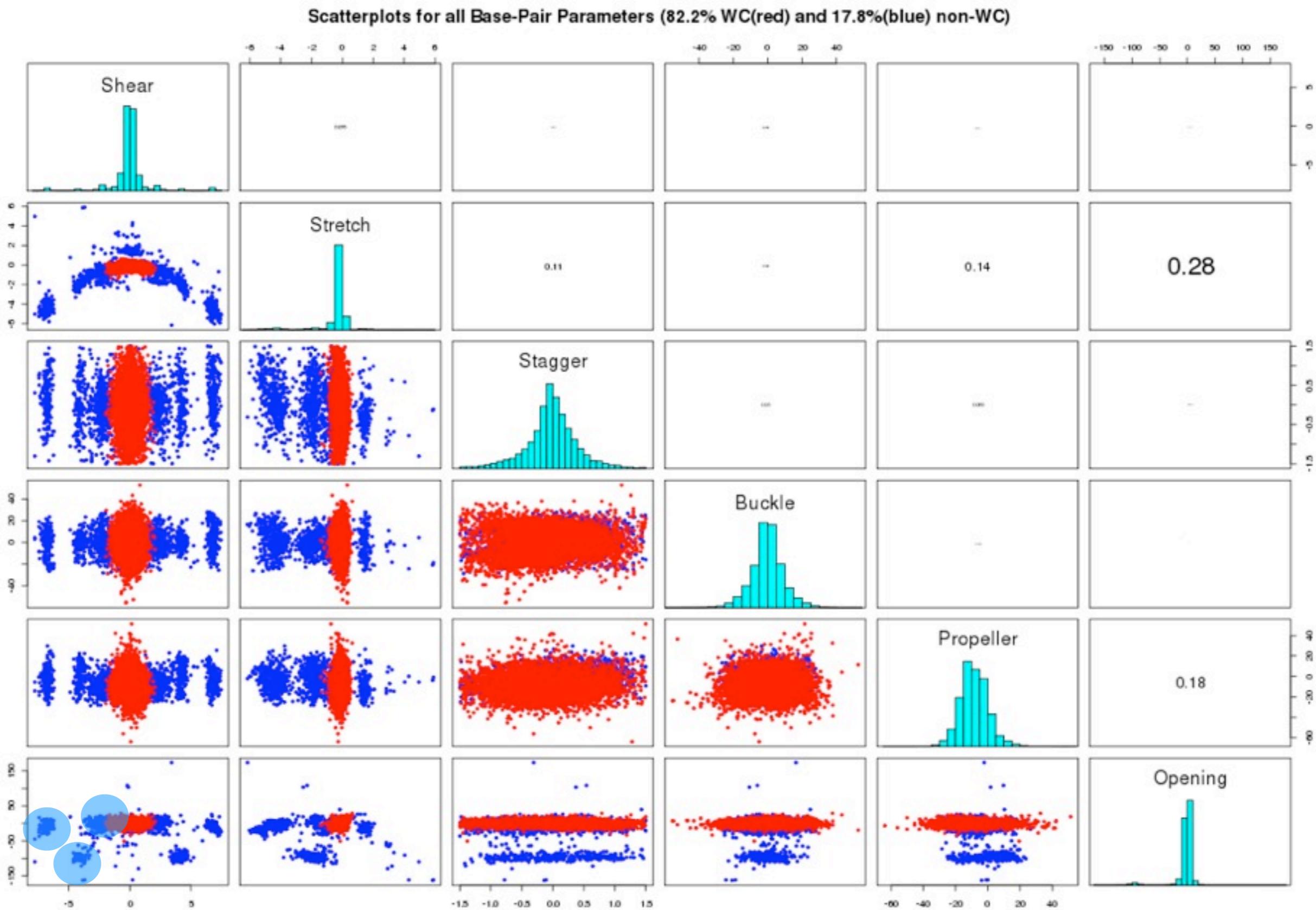
NON-CANONICAL BASE-PAIRS AND MULTIPLE BASE INTERACTIONS

seven most predominant
base-pairs in RNA

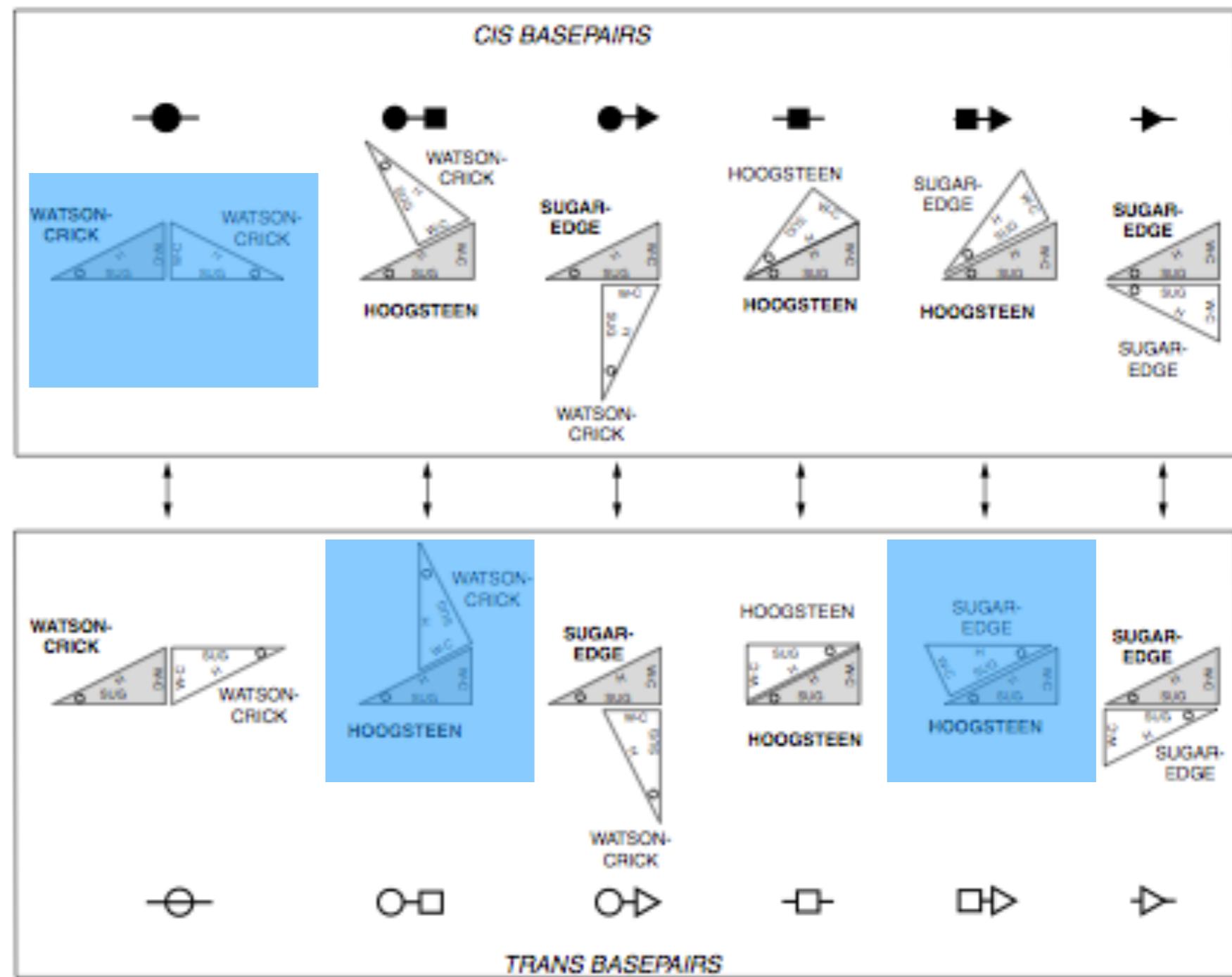
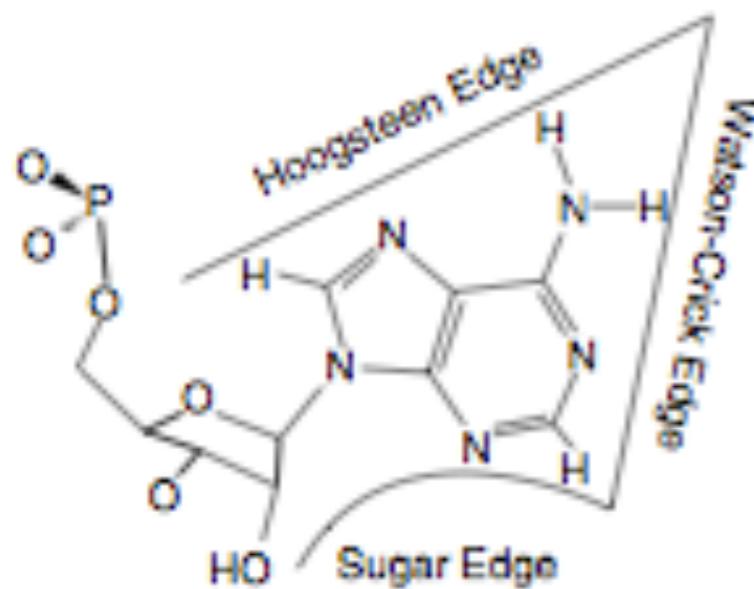
pentuplet from
the ribosome



RNA BASE-PAIRS ARE MAINLY DEFORMED VIA SHEAR AND OPENING



THE MOST PREDOMINANT BASE-PAIRS IN RNA ARE CIS W/W, TRANS H/S AND TRANS H/W



UNIQUE BASE-PAIR STEPS IN RNA CAN BE MORE THAN TEN

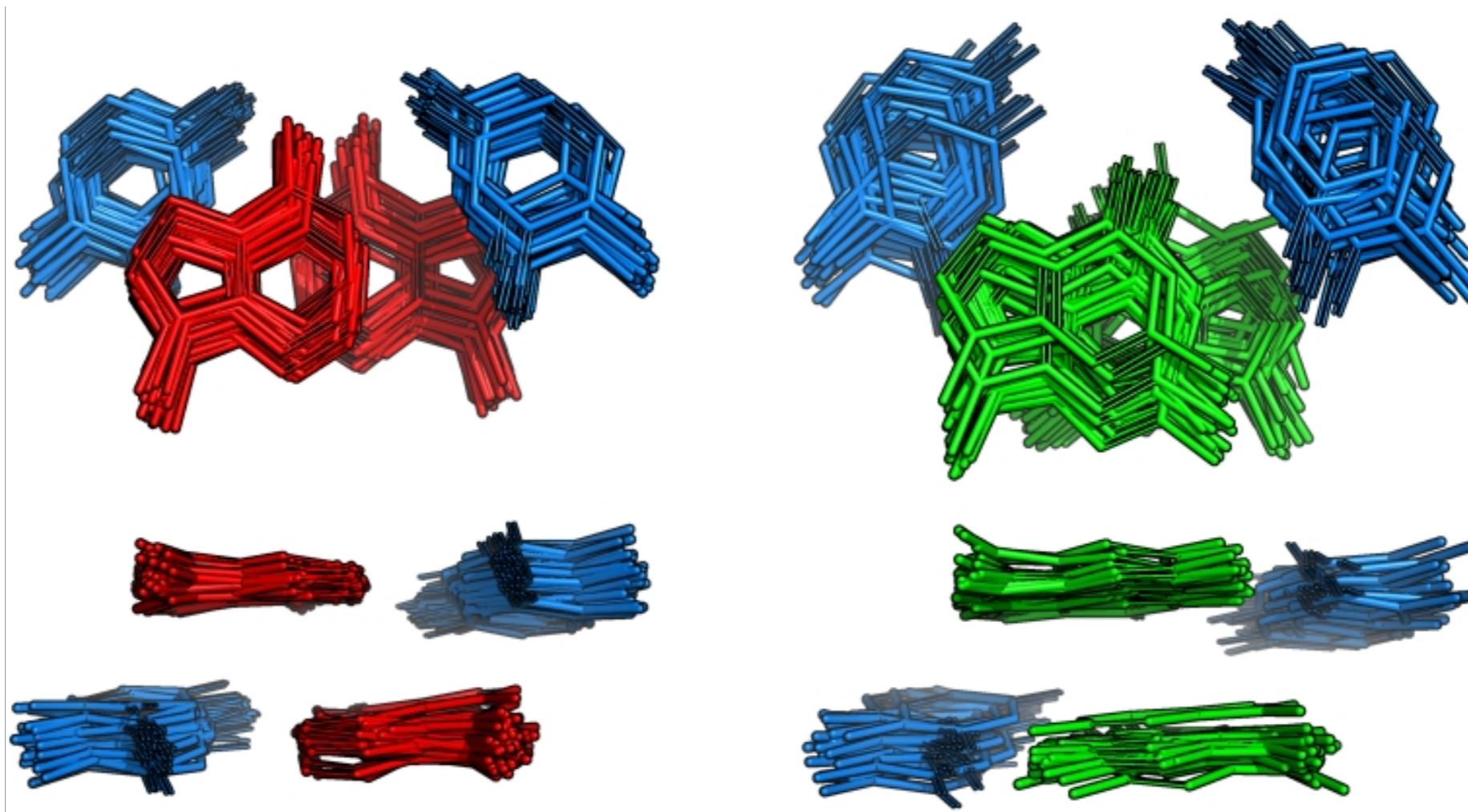
| $i \backslash i+1$ | A·U | U·A | G·C | C·G | G·U | U·G |
|--------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|-----------------------------|
| U·A | 5' U·A 3' ↓ A·U 3' 5' | 5' U·A 3' ↓ U·A 3' 5' | 5' U·A 3' ↓ G·C 3' 5' | 5' U·A 3' ↓ C·G 3' 5' | 5' U·A 3' ↓ G·U 3' 5' | 5' U·A 3' ↓ U·G 3' 5' |
| A·U | 5' A·U 3' ↓ A·U 3' 5' | 5' A·U 3' ↓ U·A 3' 5' | 5' A·U 3' ↓ G·C 3' 5' | 5' A·U 3' ↓ C·G 3' 5' | 5' A·U 3' ↓ G·U 3' 5' | 5' A·U 3' ↓ U·G 3' 5' |
| G·C | 5' C·G 3' ↓ A·U 3' 5' | 5' C·G 3' ↓ U·A 3' 5' | 5' C·G 3' ↓ G·C 3' 5' | 5' C·G 3' ↓ C·G 3' 5' | 5' C·G 3' ↓ G·U 3' 5' | 5' C·G 3' ↓ U·G 3' 5' |
| C·G | 5' G·C 3' ↓ A·U 3' 5' | 5' G·C 3' ↓ U·A 3' 5' | 5' G·C 3' ↓ G·C 3' 5' | 5' G·C 3' ↓ C·G 3' 5' | 5' G·C 3' ↓ G·U 3' 5' | 5' G·C 3' ↓ U·G 3' 5' |
| U·G | 5' U·G 3' ↓ A·U 3' 5' | 5' U·G 3' ↓ U·A 3' 5' | 5' U·G 3' ↓ G·C 3' 5' | 5' U·G 3' ↓ C·G 3' 5' | 5' U·G 3' ↓ G·U 3' 5' | 5' U·G 3' ↓ U·G 3' 5' |
| GU | 5' GU 3' ↓ A·U 3' 5' | 5' GU 3' ↓ U·A 3' 5' | 5' GU 3' ↓ G·C 3' 5' | 5' GU 3' ↓ C·G 3' 5' | 5' GU 3' ↓ G·U 3' 5' | 5' GU 3' ↓ U·G 3' 5' |

USE OF 3DNA ON X-RAY STRUCTURES AND PARAMETER ANALYSIS

- With average base-pair-step parameters, average base-pair steps can be rebuilt.
- Go to <http://rnasteps.rutgers.edu>, download parameters and rebuild in <http://w3dna.rutgers.edu>.

| RNA BASE-PAIR STEP PARAMETERS | | | | | | | | | | |
|---|-------|-------|-------|-------|------|------|------|-------|--------|------|
| Stack Type | Step | Count | Shift | Slide | Rise | Tilt | Roll | Twist | Volume | RMSD |
| RR | GG.CC | 1274 | -0.01 | -1.85 | 3.30 | 0.0 | 7.4 | 31.1 | 2.0 | 0.35 |
| YR | UG.CA | 700 | 0.03 | -1.59 | 3.16 | 0.2 | 10.6 | 30.7 | 1.2 | 0.31 |
| RY | GC.GC | 587 | 0.02 | -1.56 | 3.20 | 0.0 | 4.2 | 33.5 | 1.3 | 0.34 |
| YR | CG.CG | 562 | 0.05 | -1.84 | 3.29 | 0.3 | 10.8 | 29.1 | 2.2 | 0.35 |
| RR | AG.CU | 547 | 0.06 | -1.66 | 3.25 | -0.1 | 8.2 | 30.1 | 0.5 | 0.35 |
| RY | AC.GU | 546 | 0.14 | -1.48 | 3.22 | 0.3 | 4.9 | 32.7 | 1.5 | 0.33 |
| RR | GA.UC | 484 | 0.02 | -1.61 | 3.20 | 0.0 | 5.9 | 32.6 | 2.2 | 0.36 |
| RR | AA.UU | 241 | -0.08 | -1.38 | 3.16 | -0.4 | 7.1 | 31.6 | 1.0 | 0.32 |
| RY | GC.GU | 237 | 0.06 | -1.25 | 3.21 | 0.0 | 4.4 | 41.4 | 0.6 | 0.28 |
| RR | GG.CU | 180 | 0.01 | -1.76 | 3.31 | -0.2 | 5.0 | 37.1 | 2.0 | 0.39 |
| « previous 1 2 3 next » | | | | | | | | | | |

DEFORMABILITY OF BASE-PAIR STEPS IN RNA IS SEQUENCE DEPENDENT



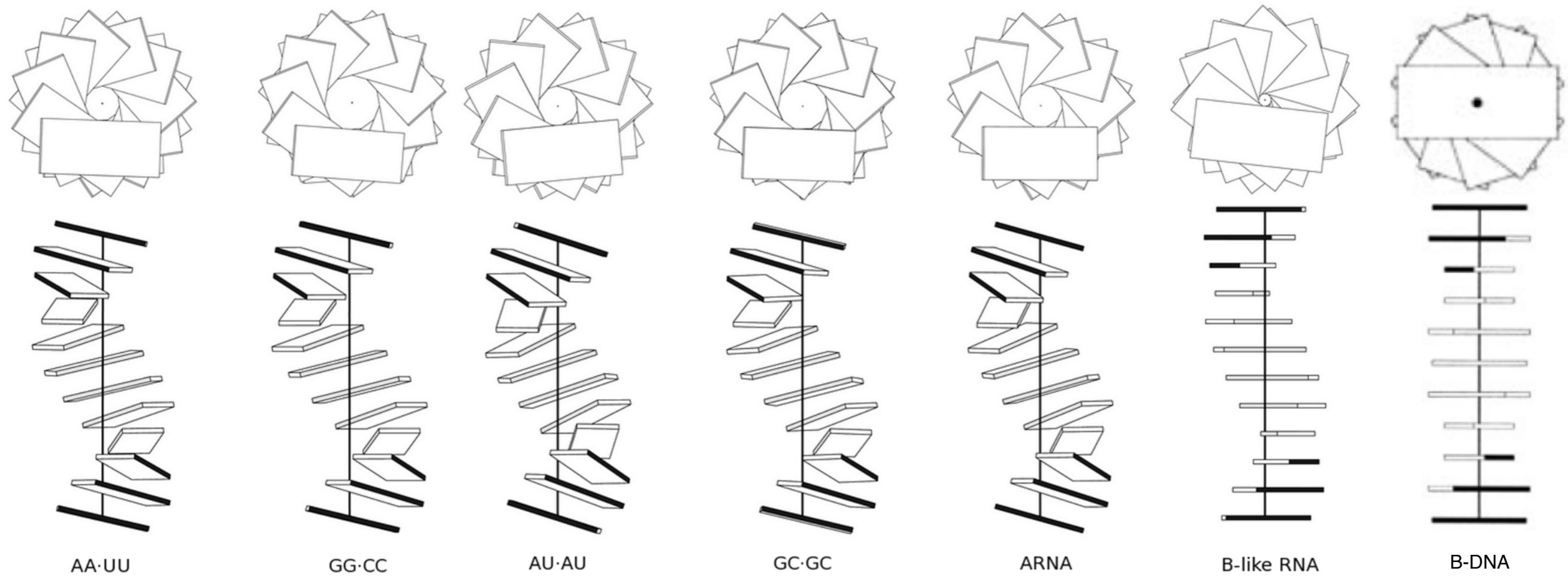
UA · UA

less deformable

UG · UG

more deformable

RNA SEQUENCE HAS SUBTLE EFFECTS ON THE STRUCTURE OF RNA



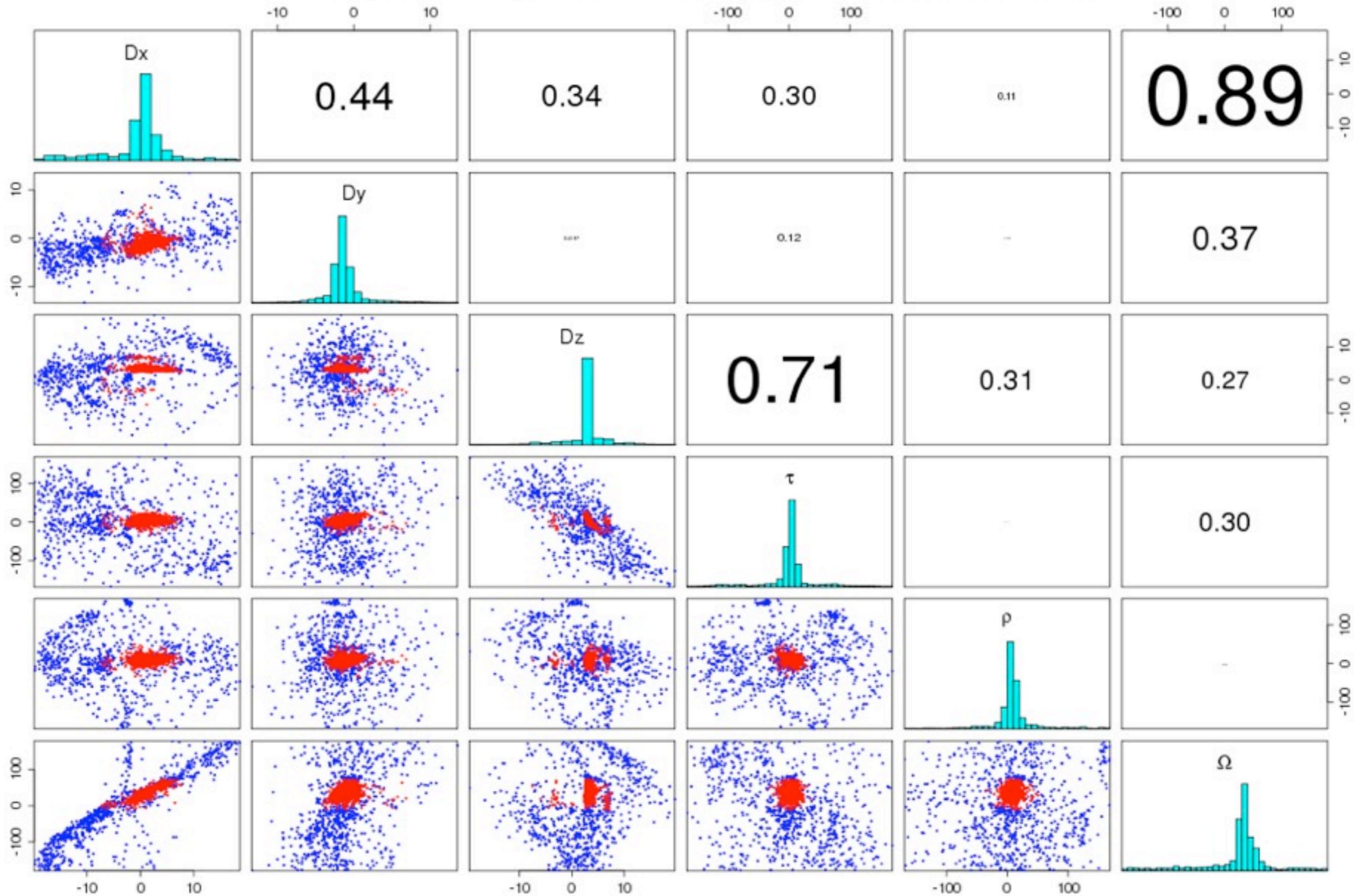
homopolymers block copolymers

slide = -1.5
rise = 3.30
tilt = 0.0
roll = 0.0
twist = 31.6

slide = 0.0
rise = 3.36
tilt = 0.0
roll = 0.0
twist = 36.0

RNA HELICAL REGIONS IN THE RIBOSOME

A-RNA (RMSD <= 18) and non-A-RNA (RMSD > 18) like base-steps



HARMONIC POTENTIAL MODEL FOR NUCLEIC ACIDS

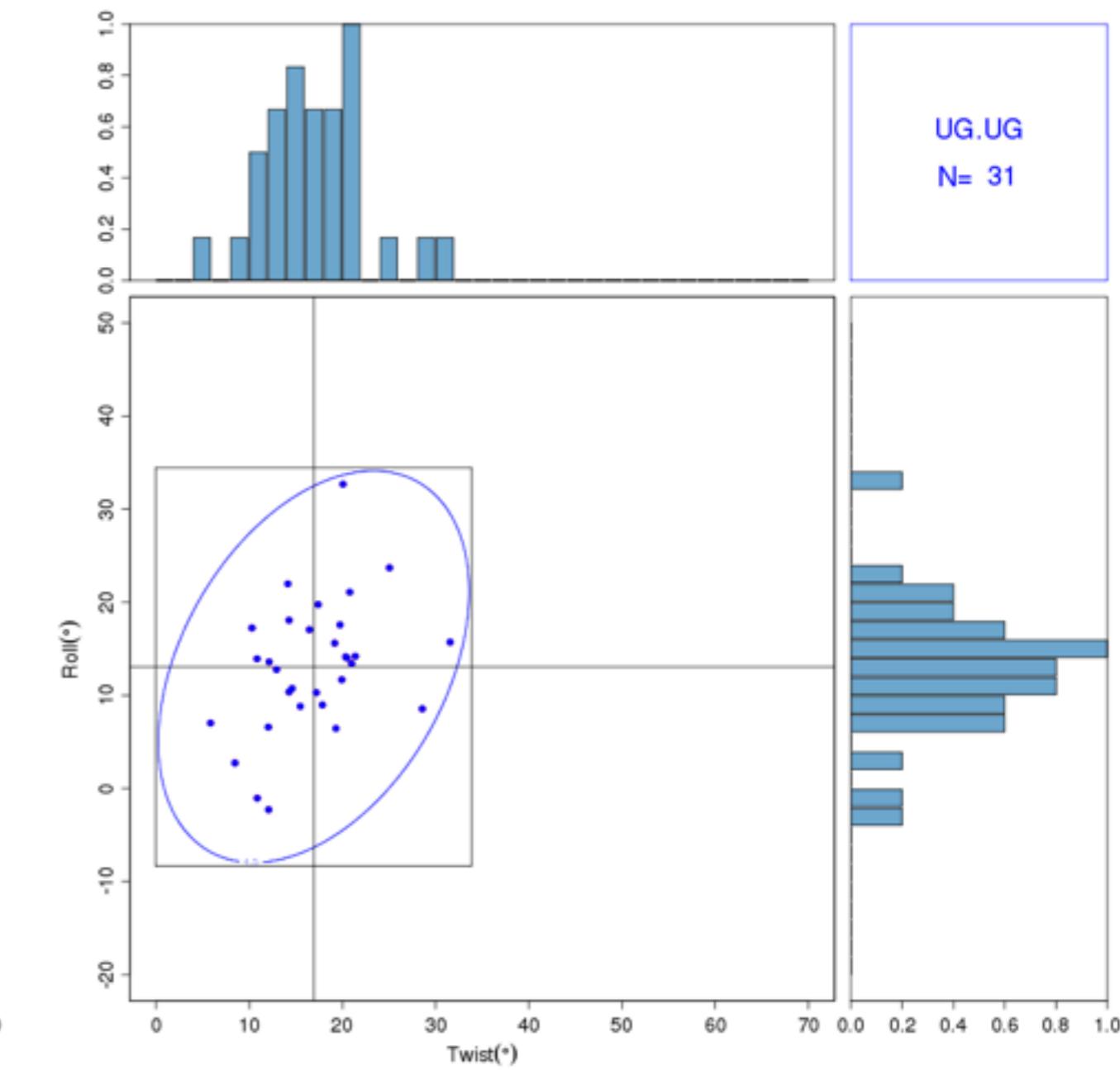
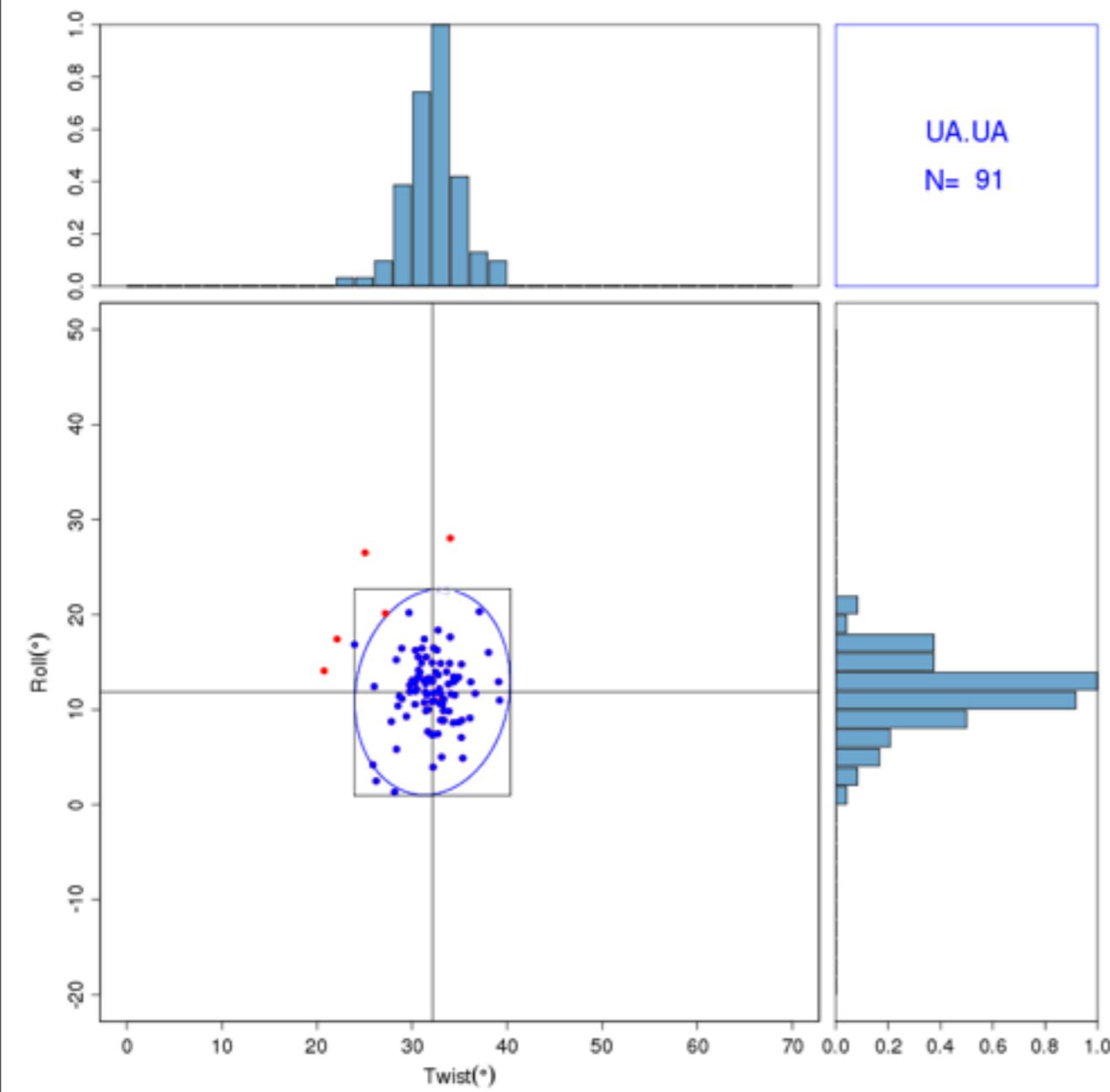
- From Base-pair step parameters, inverse covariance matrix and you get analog to force-constant matrix.
- With force constants you can make a simple spring model, your good ole Hooke's law in sixth dimension.

$$\Psi = \frac{1}{2} \sum_{i,j} F_{ij} \Delta x_i \Delta x_j$$

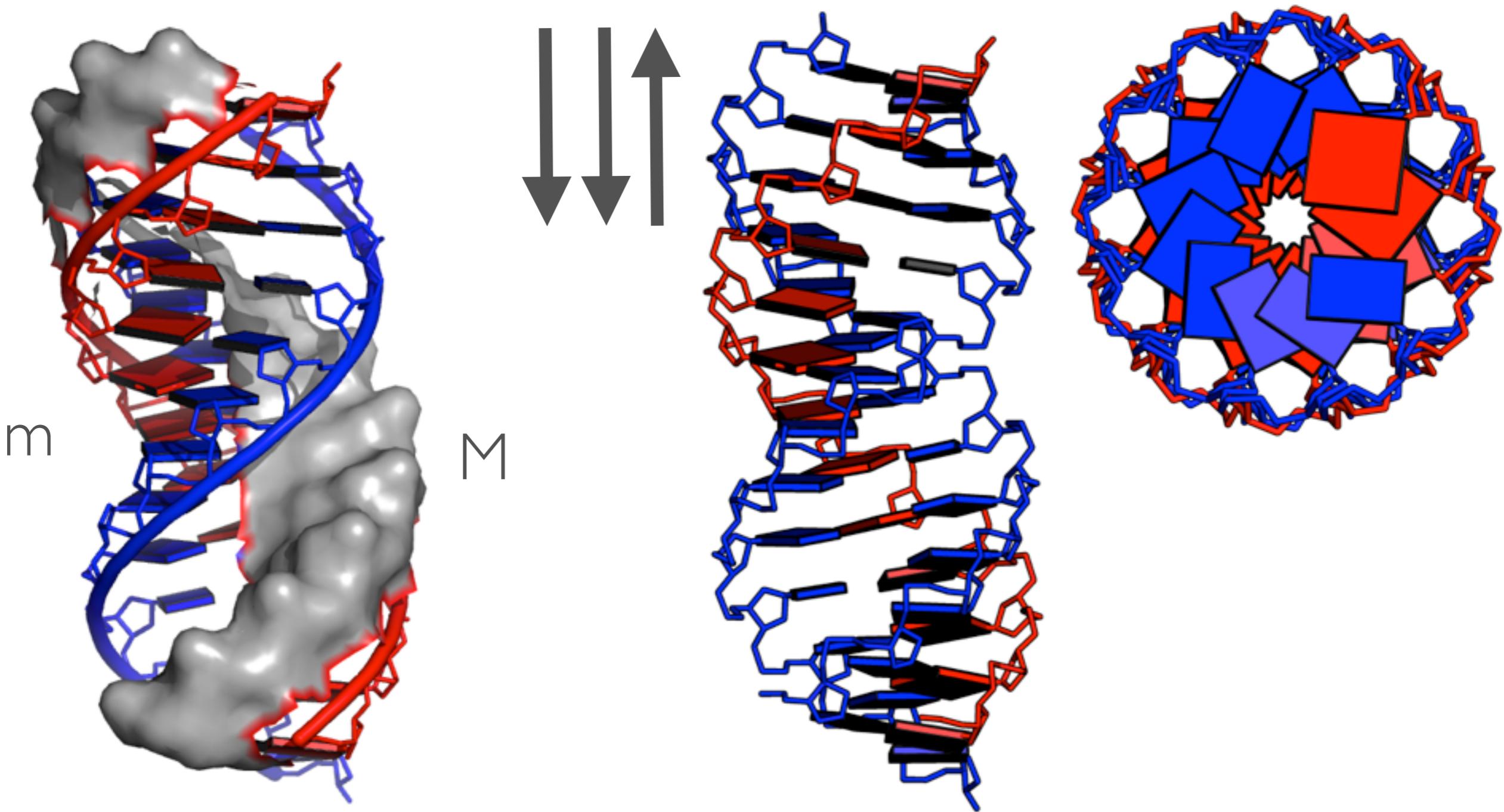
$$(\Delta x_i = x_i - x_{i0})$$

$$U = \sum_{n=1}^N \Psi_n$$

HARMONIC POTENTIALS FOR RNA BASE-PAIR STEPS SHOW SEQUENCE PREFERENCES



DNA TRIPLE HELICES WITH BLOCVIEW



USE AND APPLICATION OF THE RIGID-BODY PARAMETER FORMALISM

- General analysis of sequence dependent properties of DNA.
- Compute deformation scores for DNA based on X-ray data standards.
- From step-parameter information and inverse covariance analysis a link can be made to global polymer properties, e.g. persistence length, J-factors (cyclization probability)
- Compute topological properties of nucleic acids, e.g. linking number, twist, writhe.

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Proceedings of the National Academy of Sciences, 1998, 95, 11163-11168

Exercises

- Create A-DNA, B-DNA, Z-DNA, A-RNA and visualize in pymol.
- Analyze A-RNA. Modify the sequence in base_step.par, rebuild with modified sequence and visualize in pymol.
- modify again base_step.par but increase the slide in a step by 2 Angstroms.
- Find multiplets in structure, then extract one, then visualize it inside the structure and isolate it using pymol.



Thursday, April 28, 2011