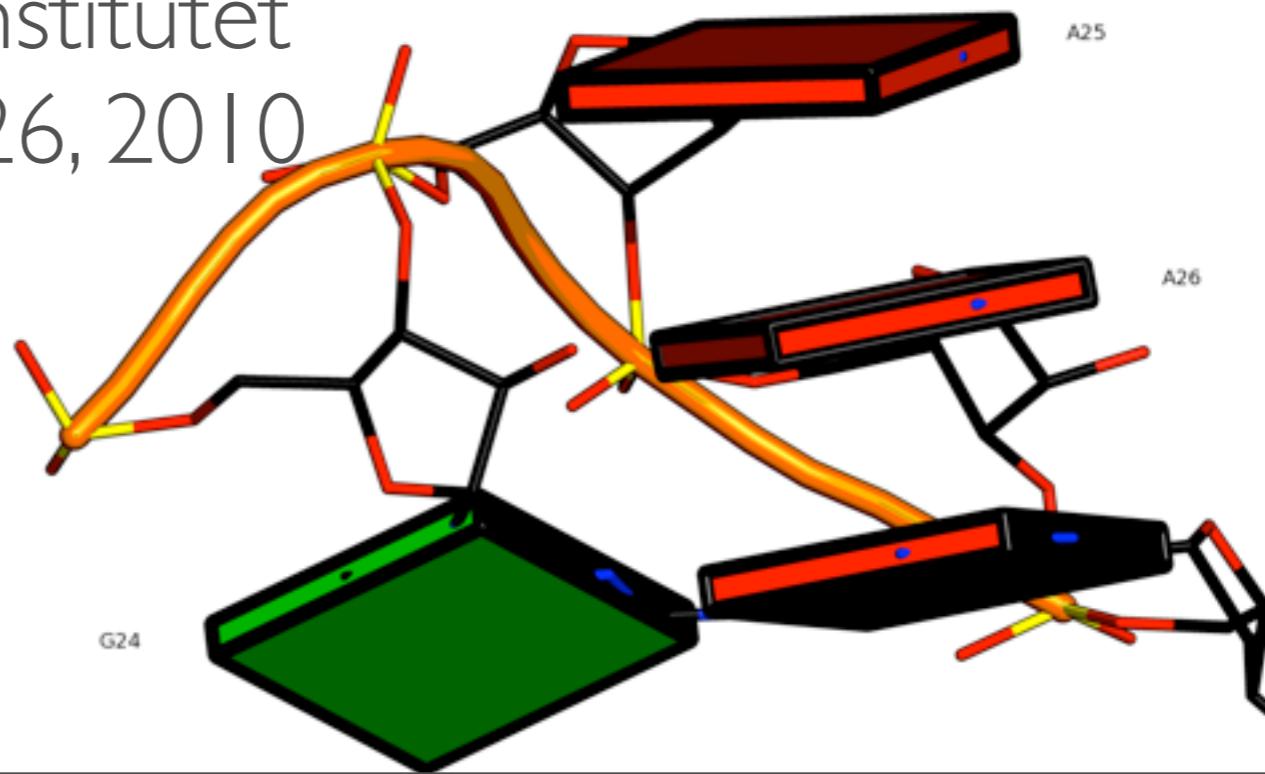


THE RIGID BODY MODEL FOR NUCLEIC ACIDS

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November 26, 2010



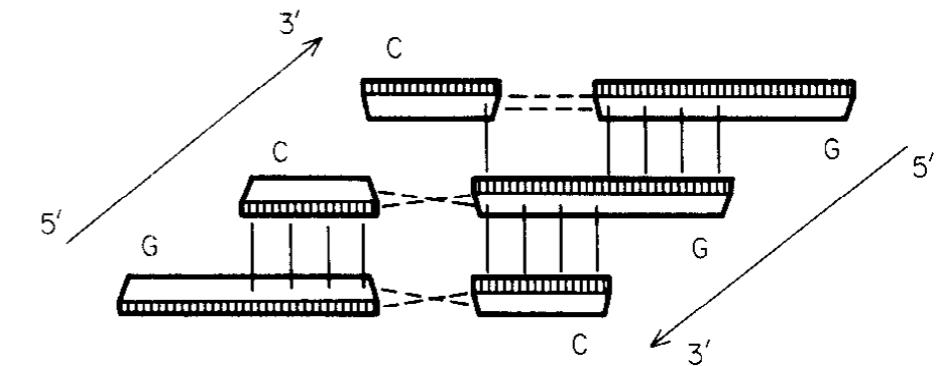
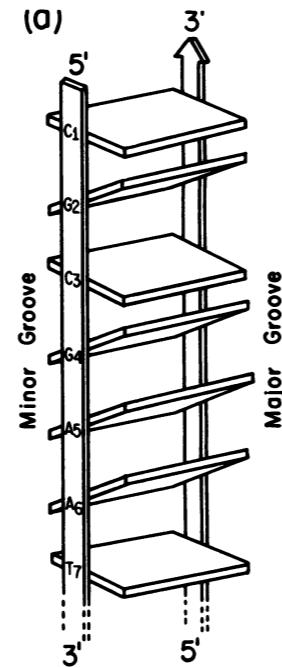
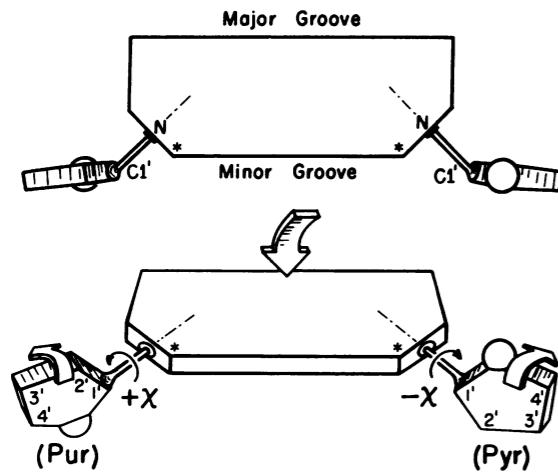
HISTORICAL OVERVIEW

- 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+



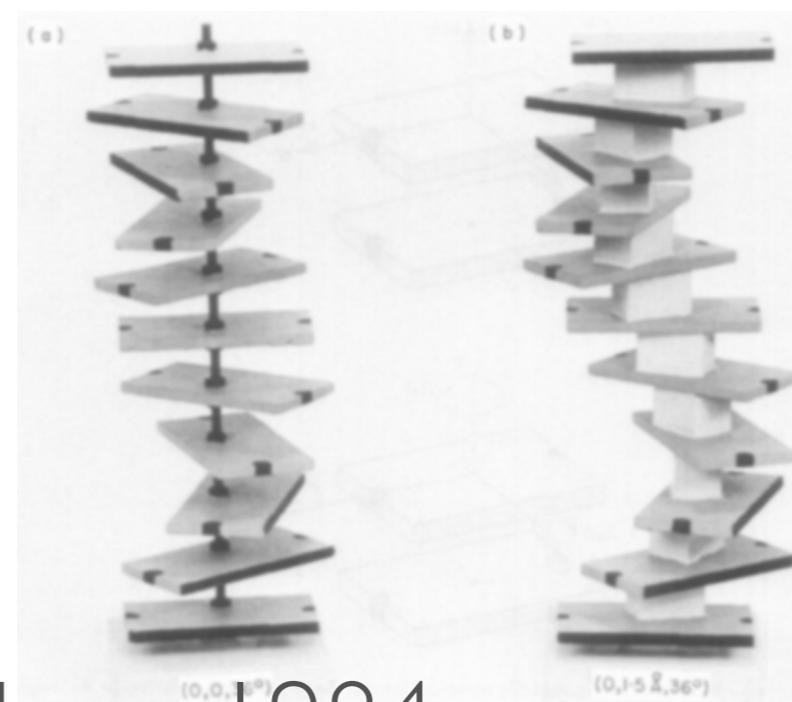
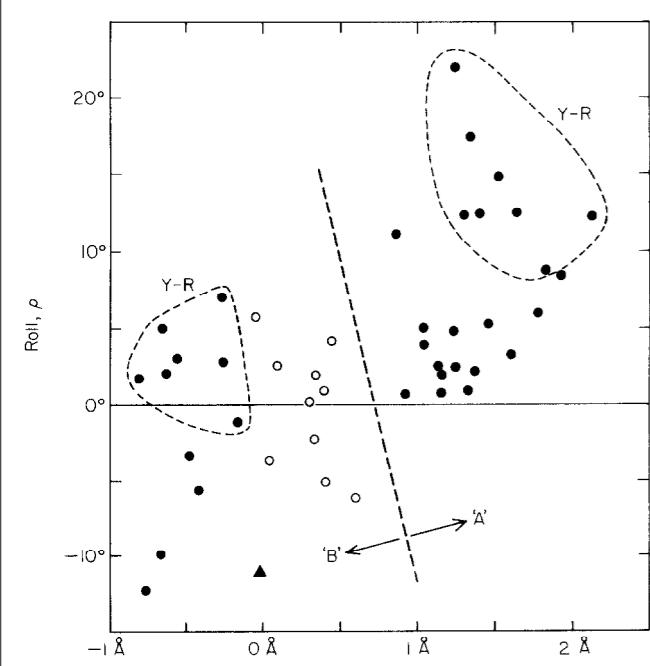
This figure is purely diagrammatic. The two ribbons symbolize the two phosphate-sugar chains, and the horizontal rods the pairs of bases holding the chains together. The vertical line marks the fibre axis

THESE ARE THE EIGHTIES FOR NUCLEIC ACIDS

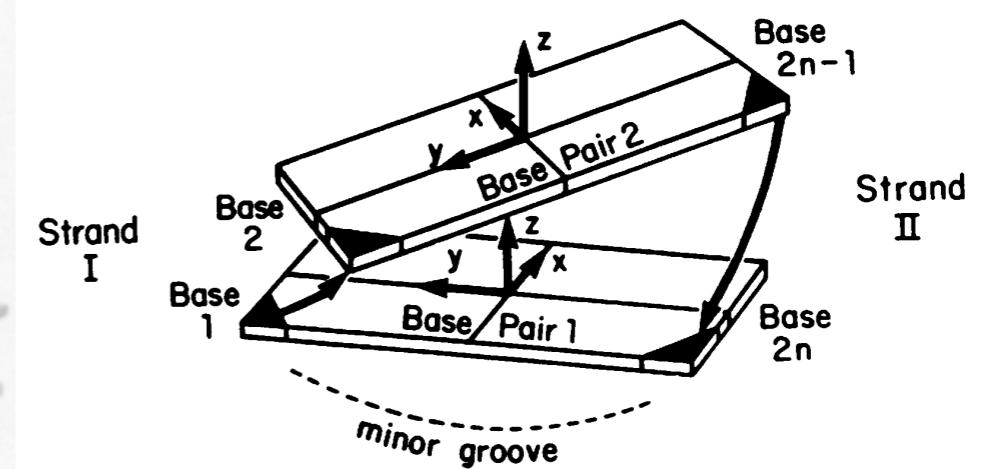


calladine-drew 1986

dickerson-drew 1981



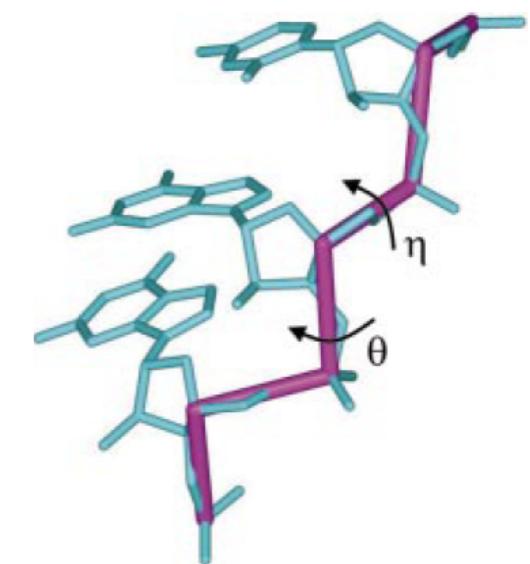
calladine-drew 1984



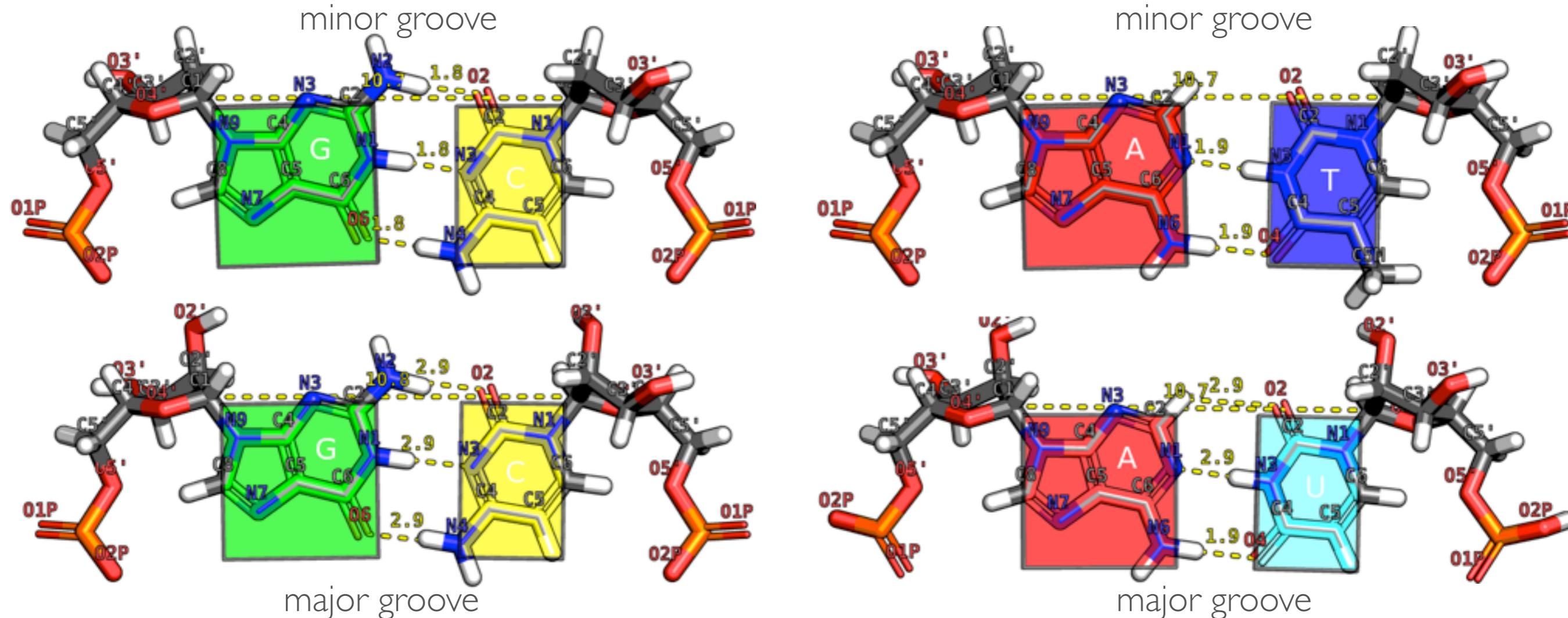
dickerson et al. 1989

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

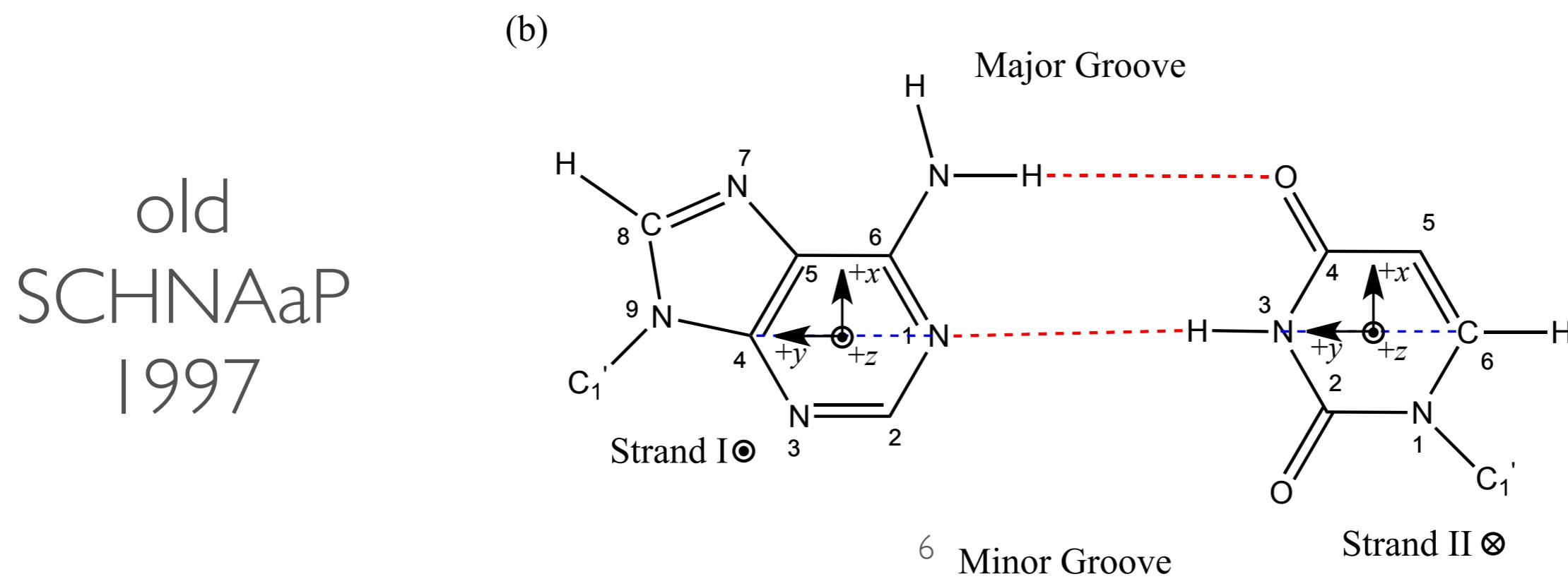
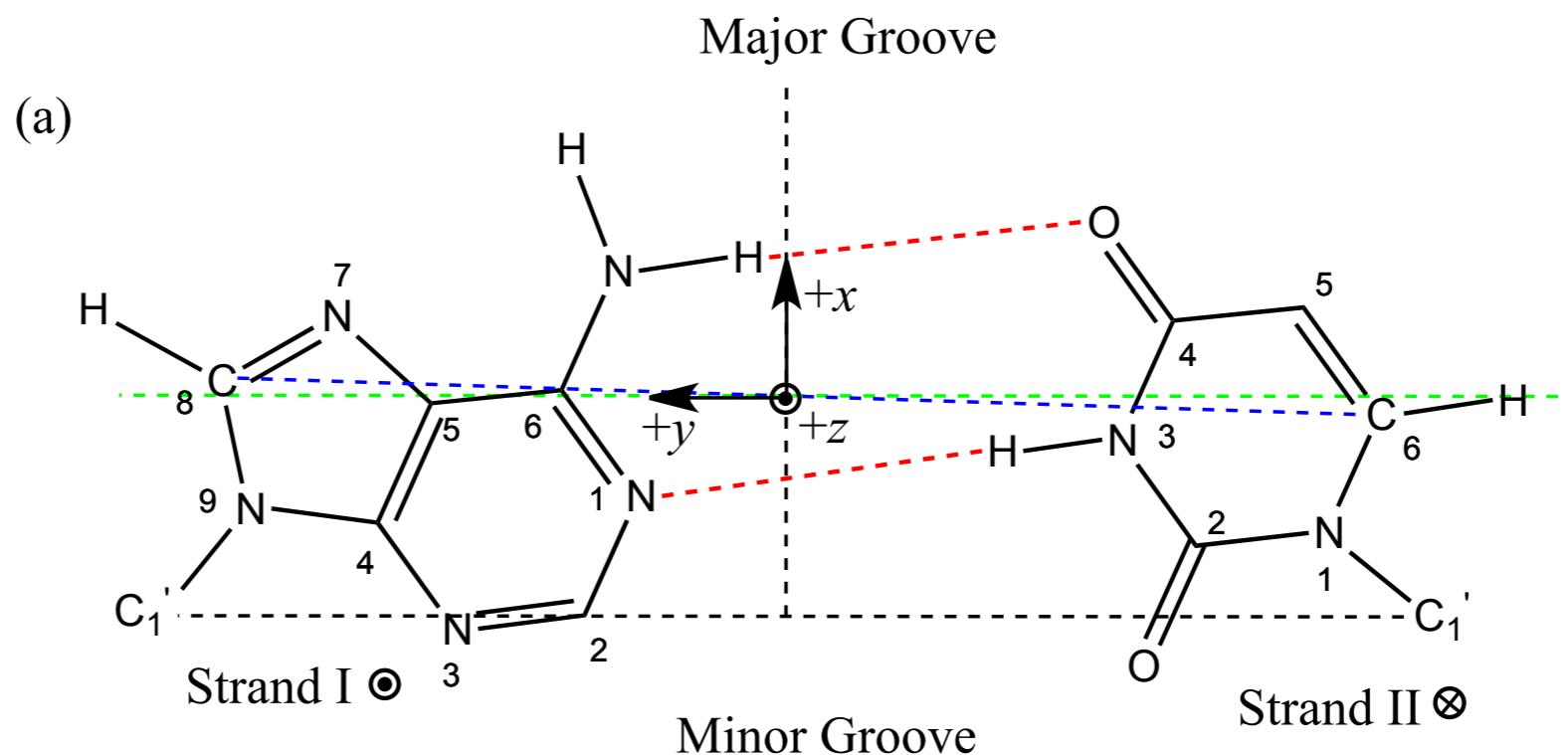


Purines aka **R** = Guanine (green) and Adenine (red)

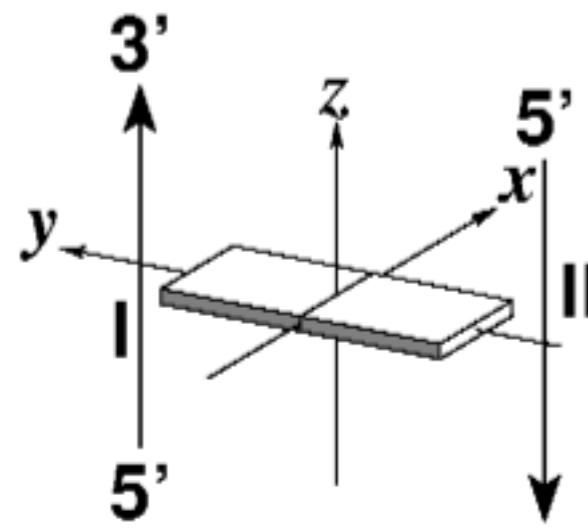
Pyrimidines aka **Y** = Cytosine (yellow), Thymine (blue) and Uracil (cyan)

STANDARD REFERENCE FRAME

new
3DNA,
Curves+
 | 1999-2001 |

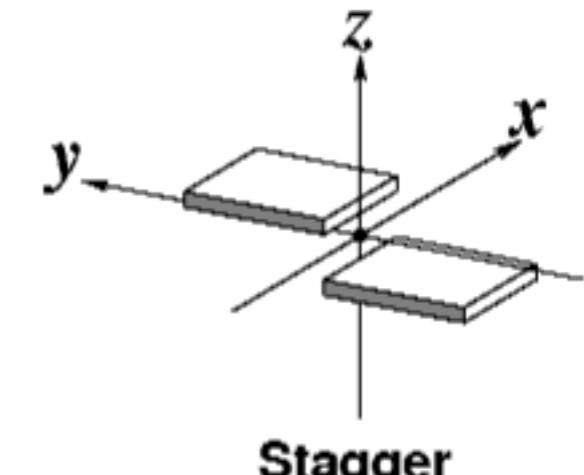
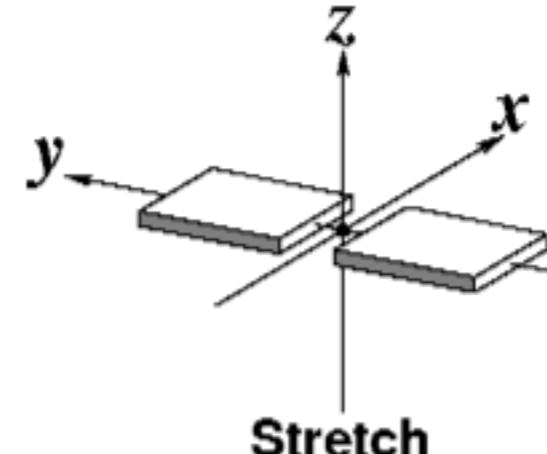
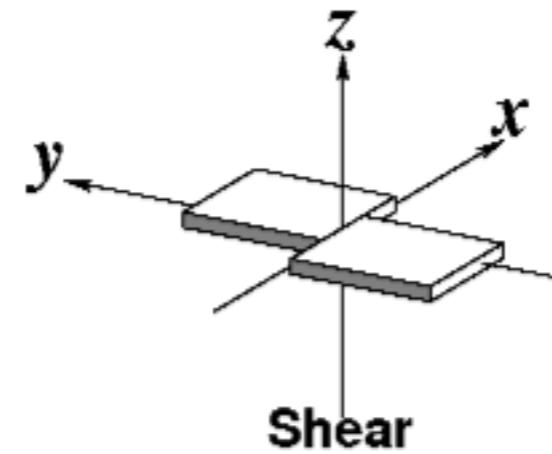


CALLADINE-DREW RIGID-BLOCK MODEL

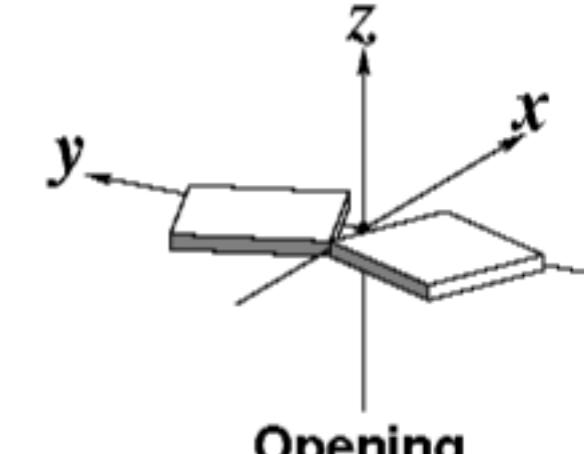
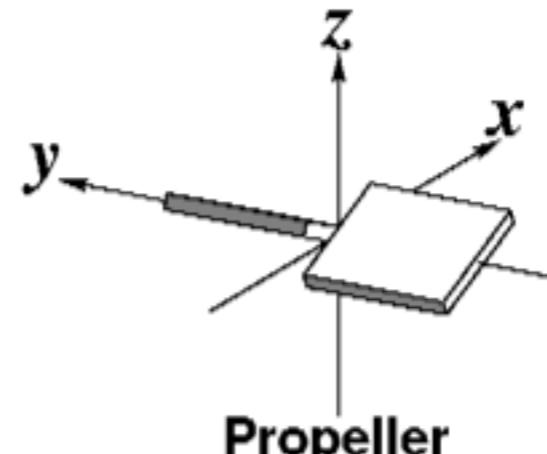
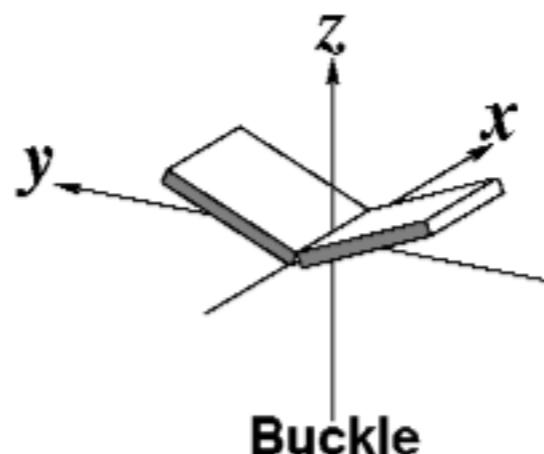


Base-Pair Parameters

translation

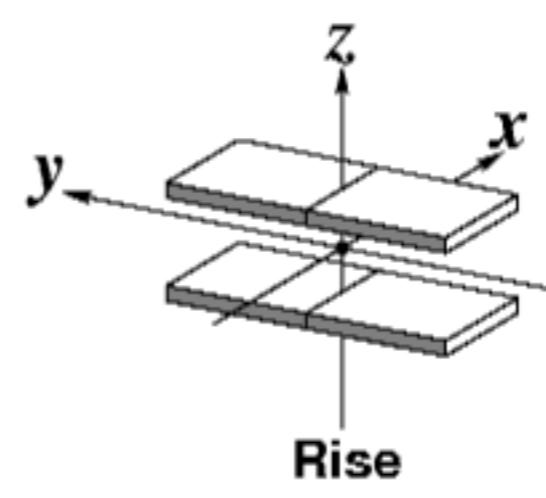
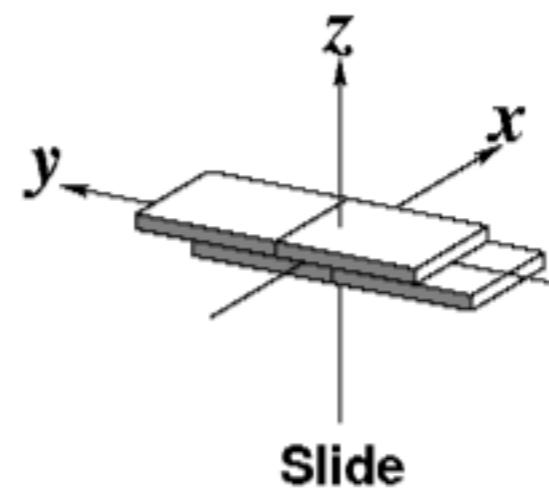
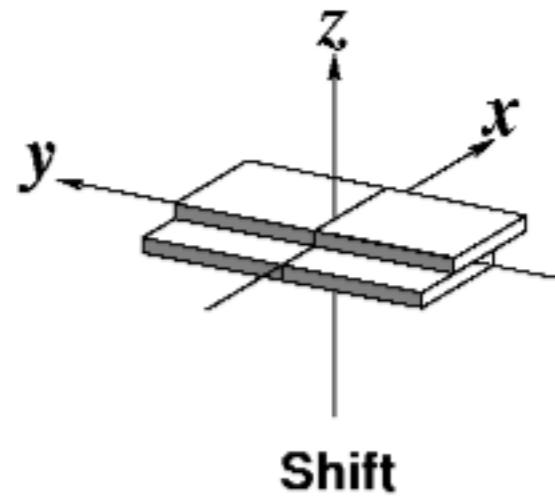


rotation

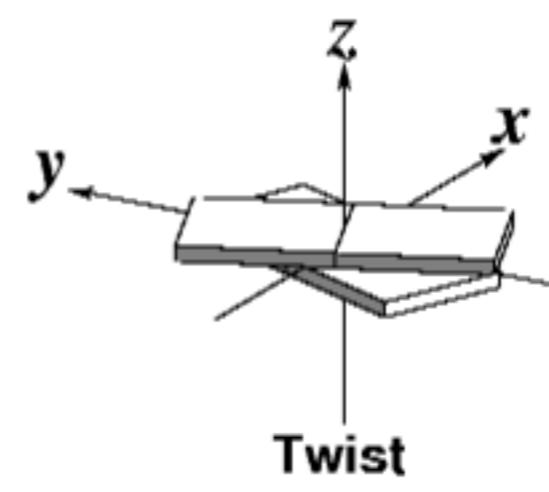
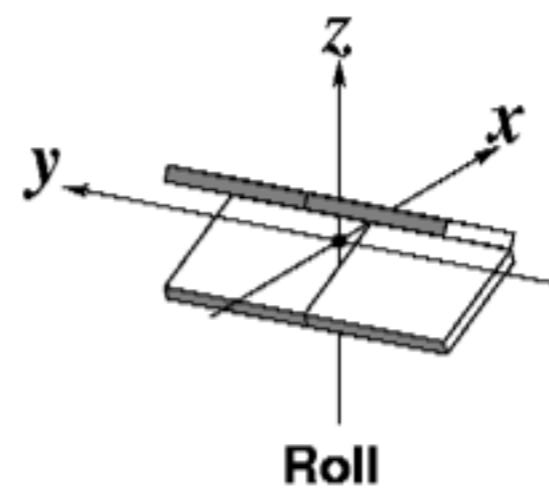
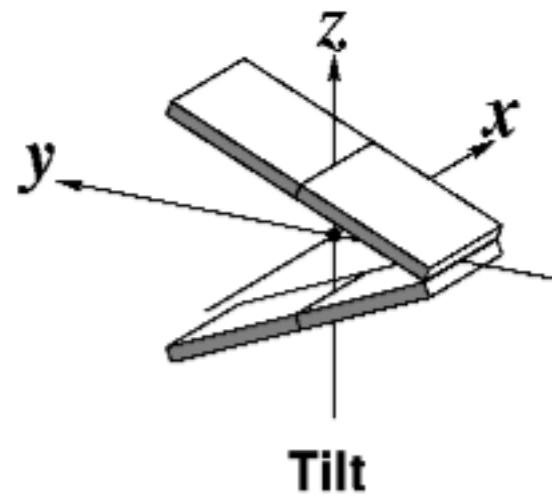


CALLADINE-DREW RIGID-BLOCK MODEL

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).

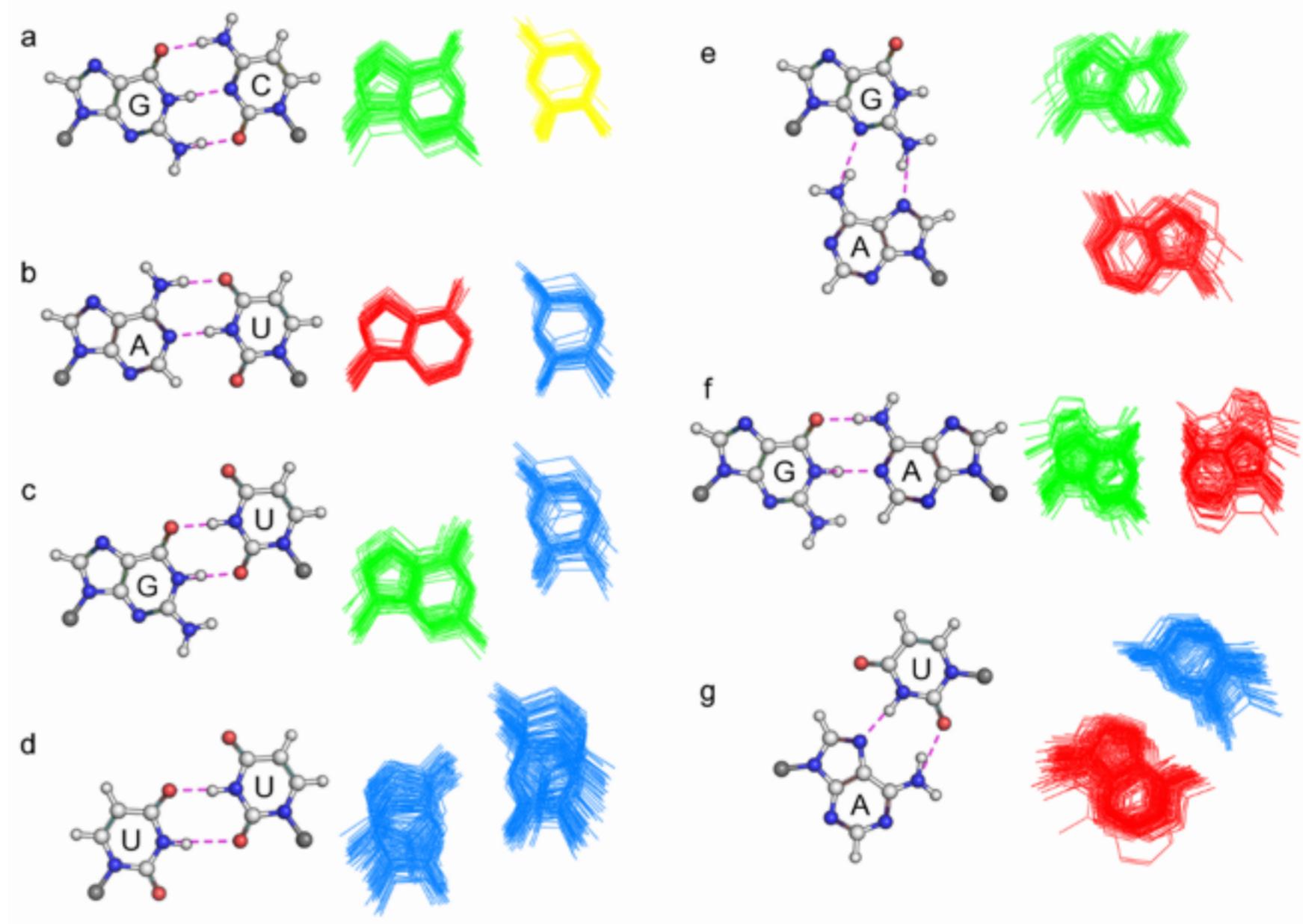
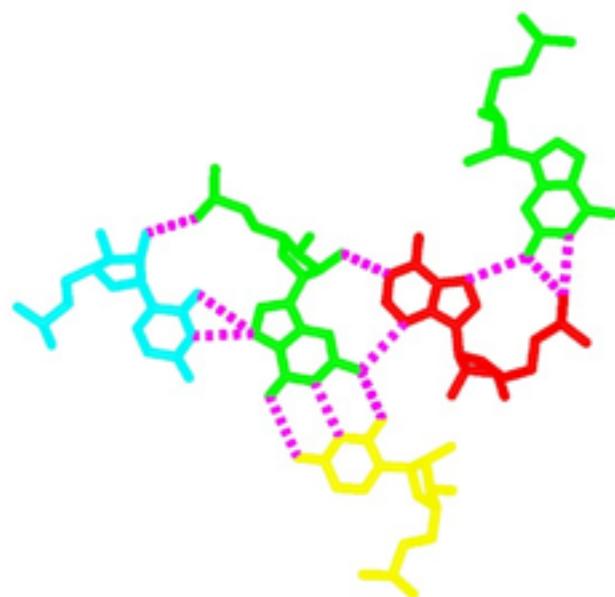
BASE-PAIR DATABASES

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

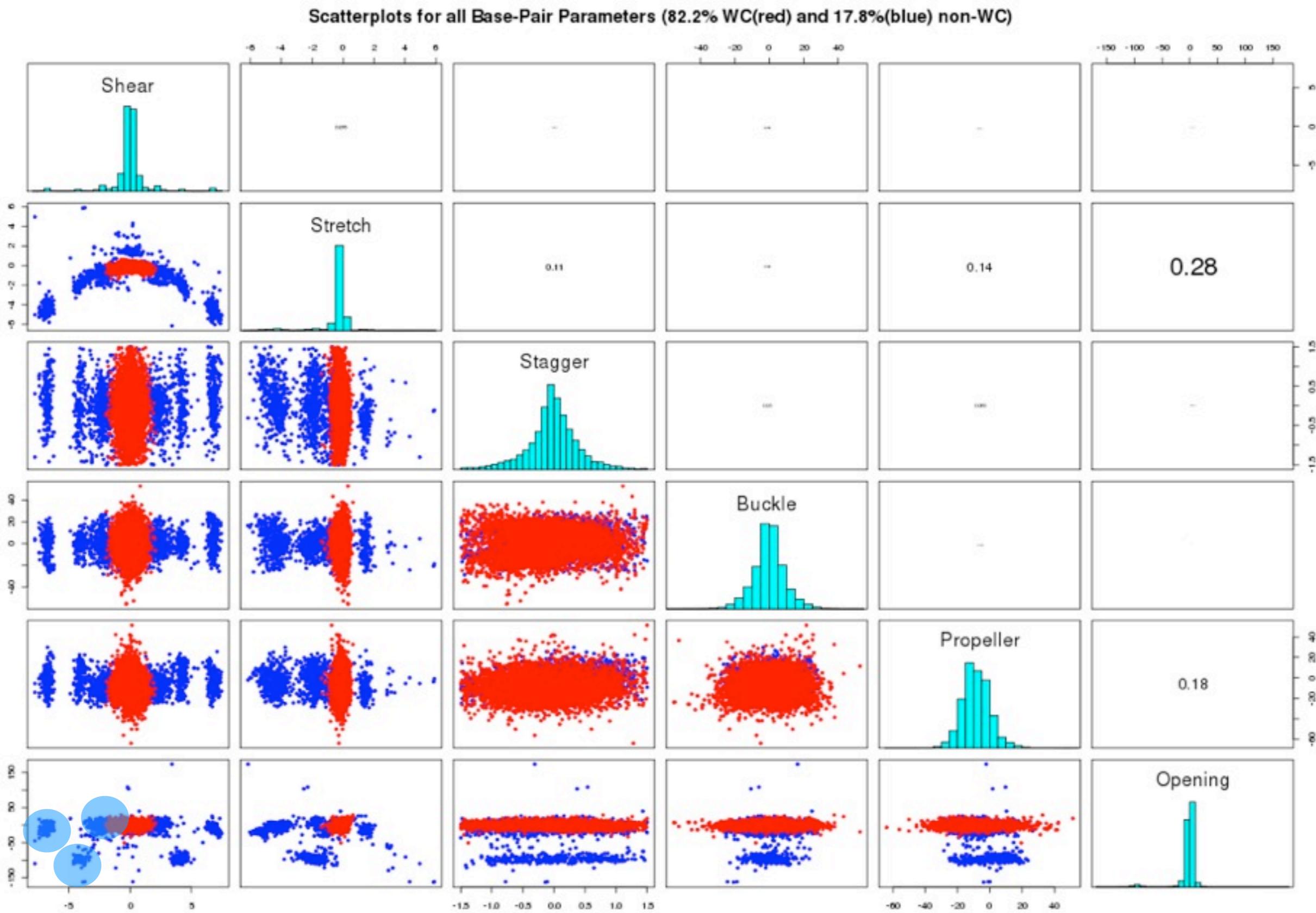
NON-CANONICAL BASE-PAIRS AND MULTIPLE BASE INTERACTIONS

seven most predominant
base-pairs in RNA

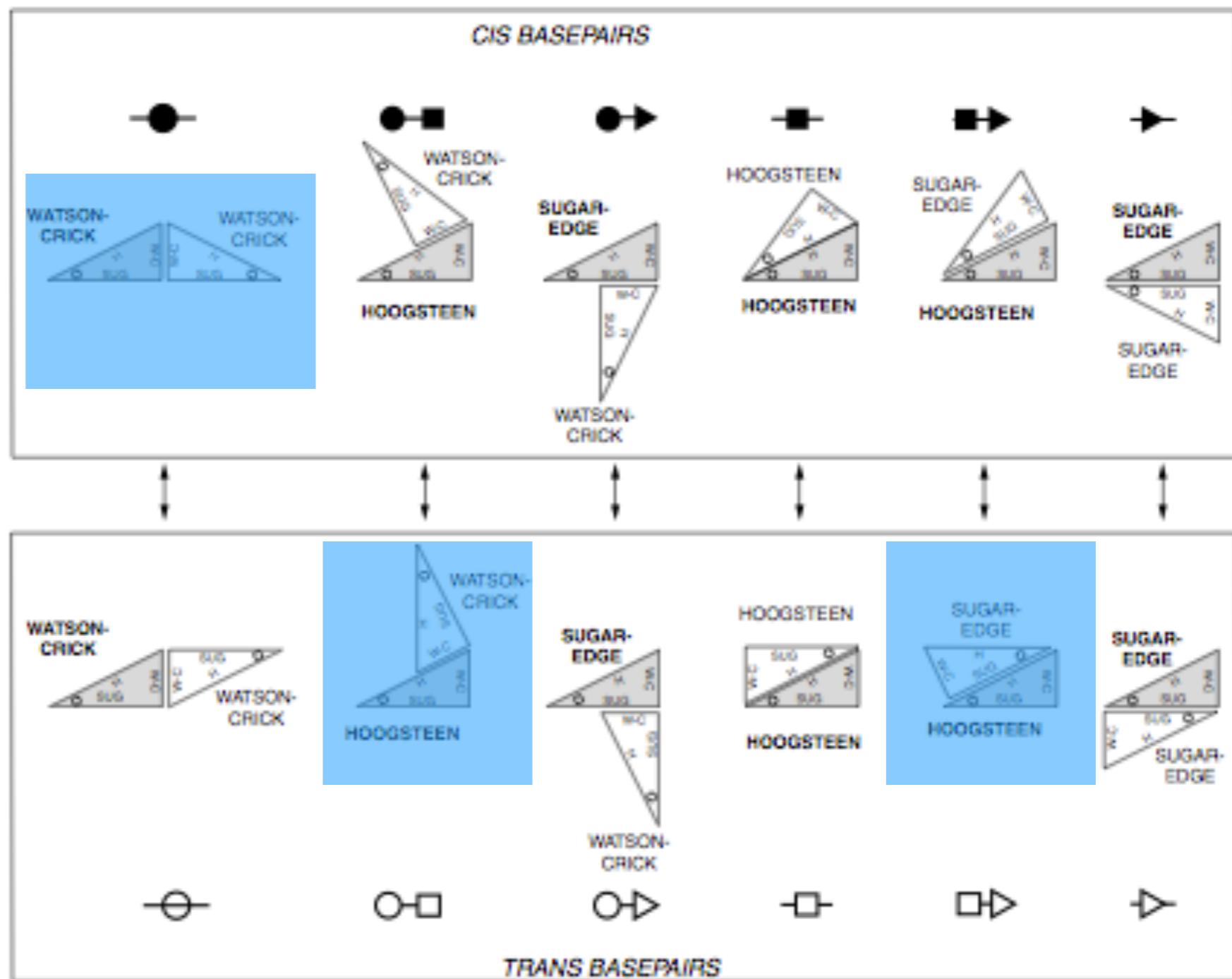
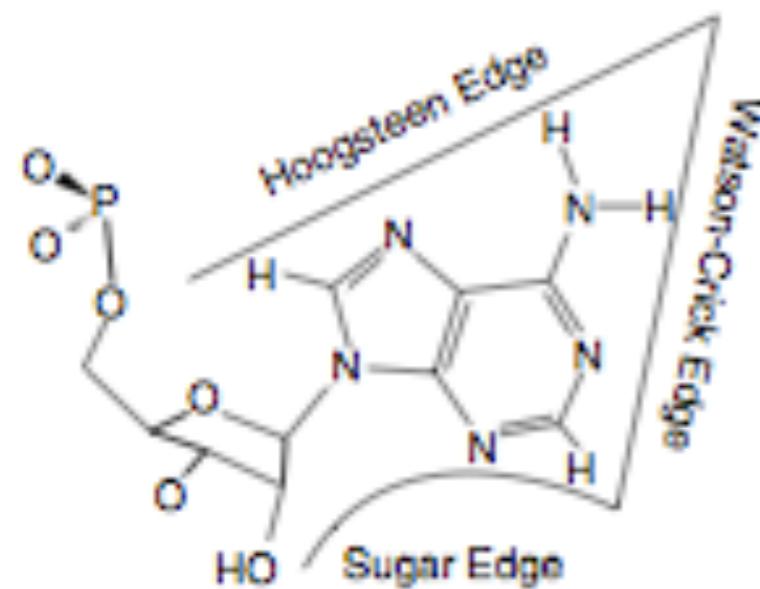
pentuplet from
the ribosome



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

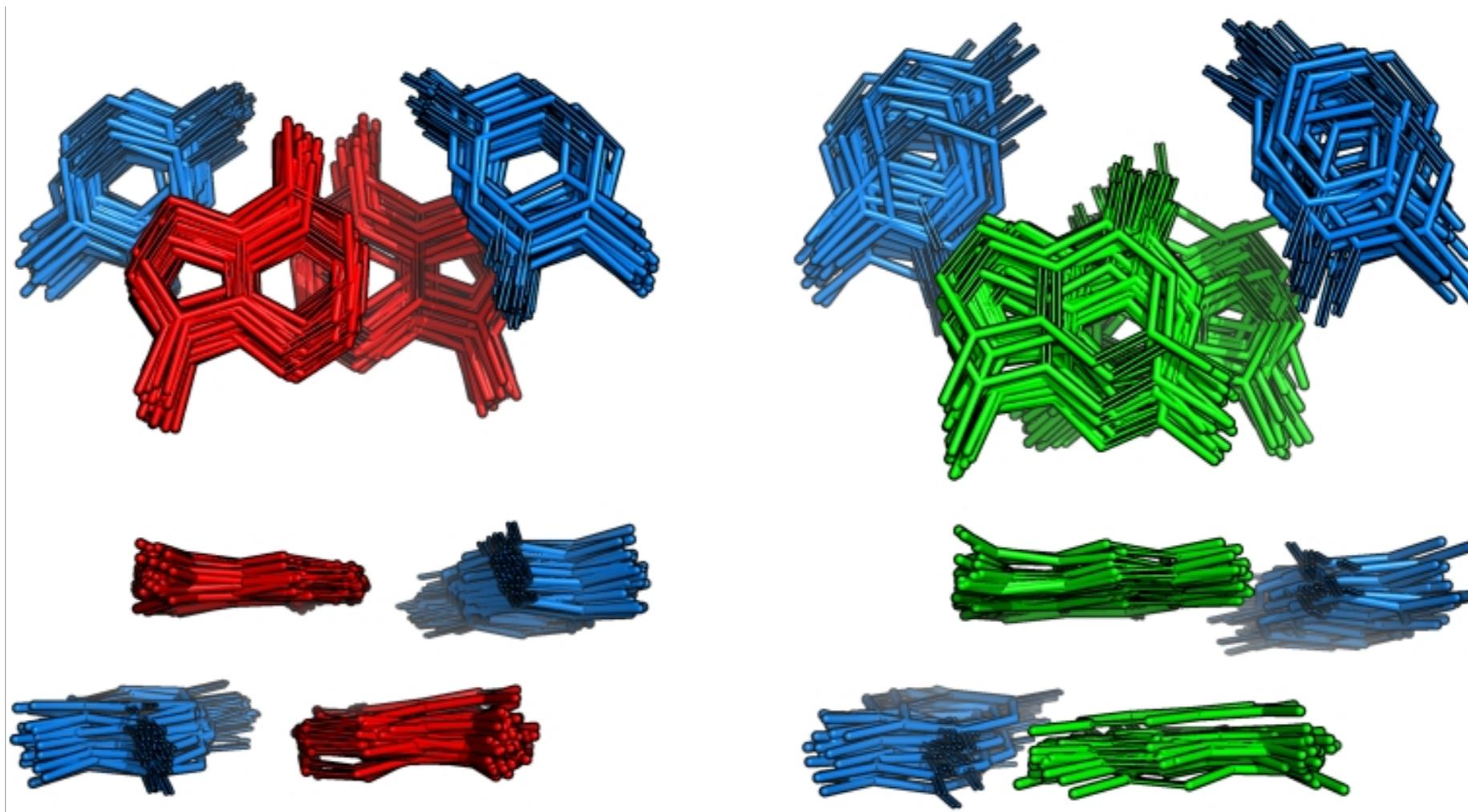
$i \backslash i+1$	A·U	U·A	G·C	C·G	G·U	U·G
U·A	5' U·A 3' ↓ A·U 3' 5'	5' U·A 3' ↓ U·A 3' 5'	5' U·A 3' ↓ G·C 3' 5'	5' U·A 3' ↓ C·G 3' 5'	5' U·A 3' ↓ G·U 3' 5'	5' U·A 3' ↓ U·G 3' 5'
A·U	5' A·U 3' ↓ A·U 3' 5'	5' A·U 3' ↓ U·A 3' 5'	5' A·U 3' ↓ G·C 3' 5'	5' A·U 3' ↓ C·G 3' 5'	5' A·U 3' ↓ G·U 3' 5'	5' A·U 3'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



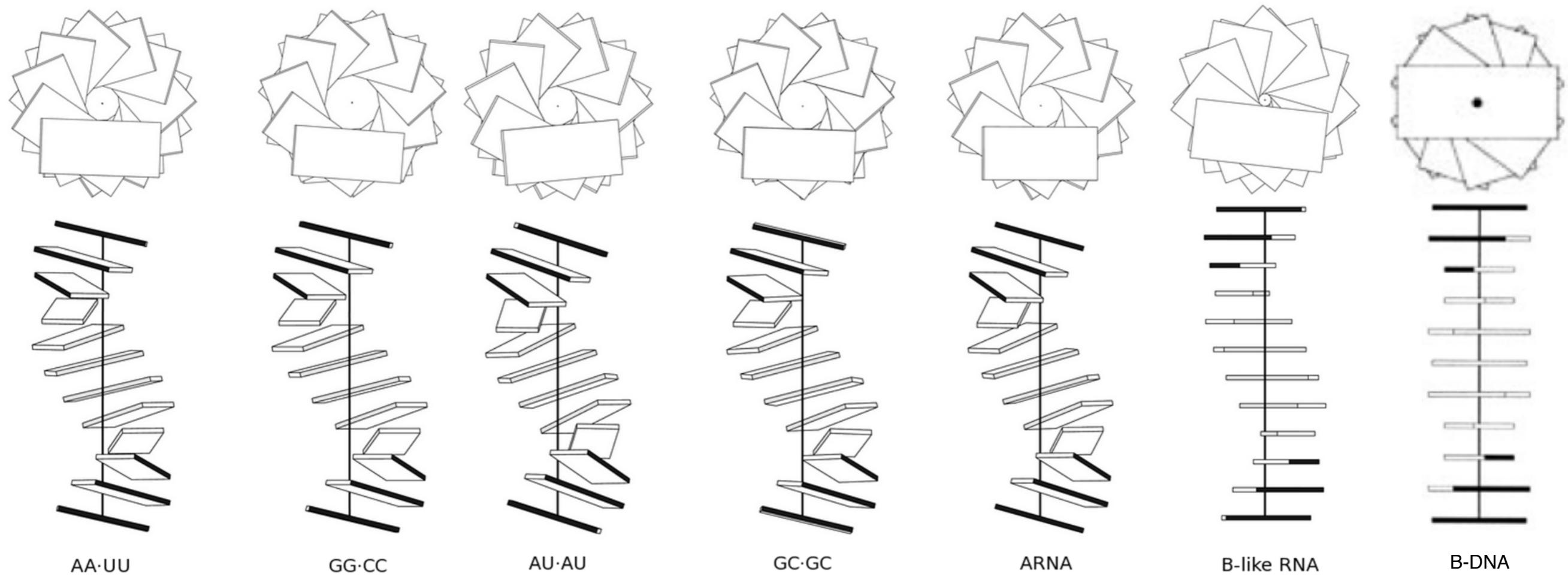
UA · UA

less deformable

UG · UG

more deformable

RNA SEQUENCE HAS SUBTLE EFFECTS ON THE STRUCTURE OF RNA



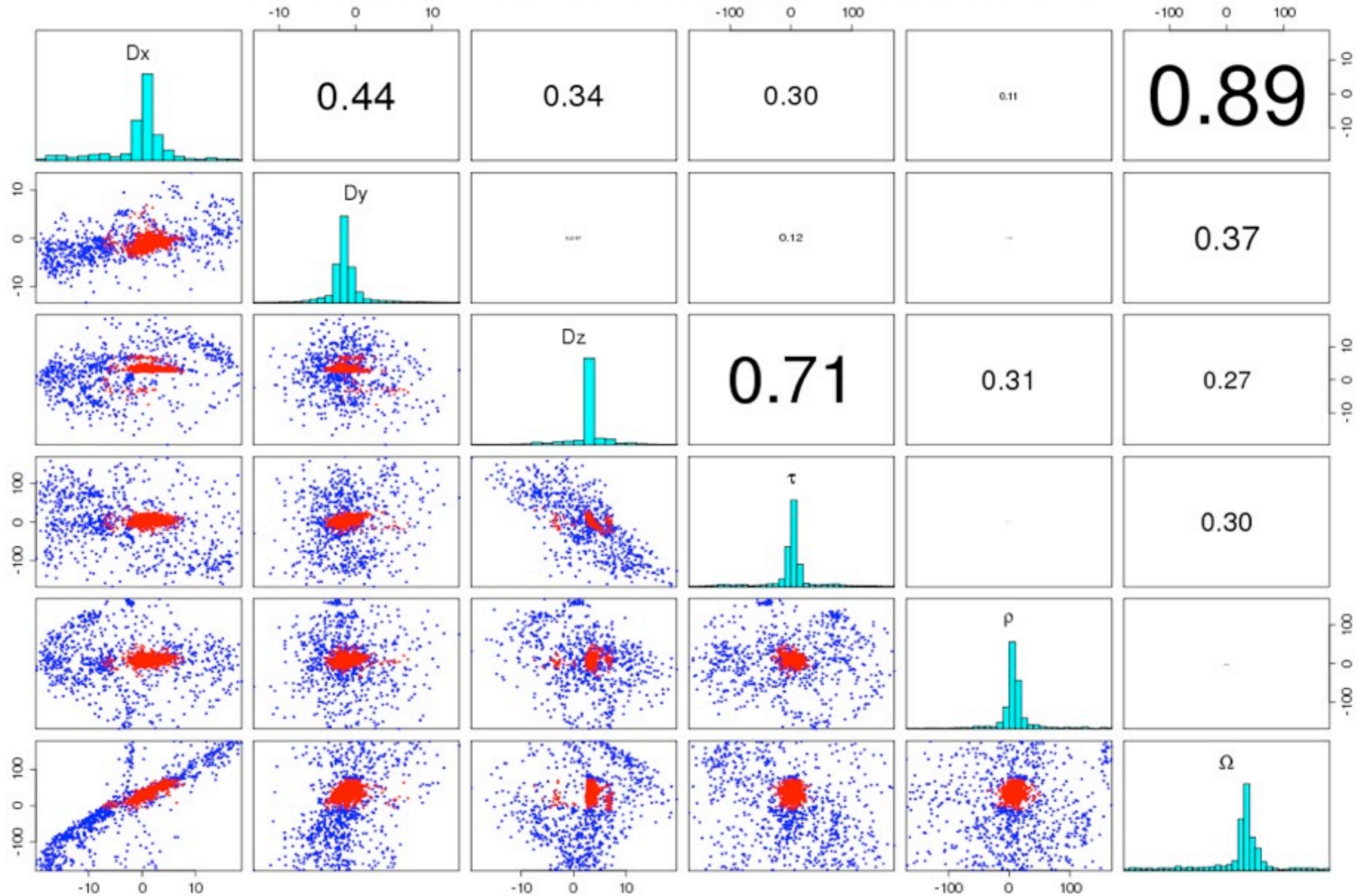
homopolymers block copolymers

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

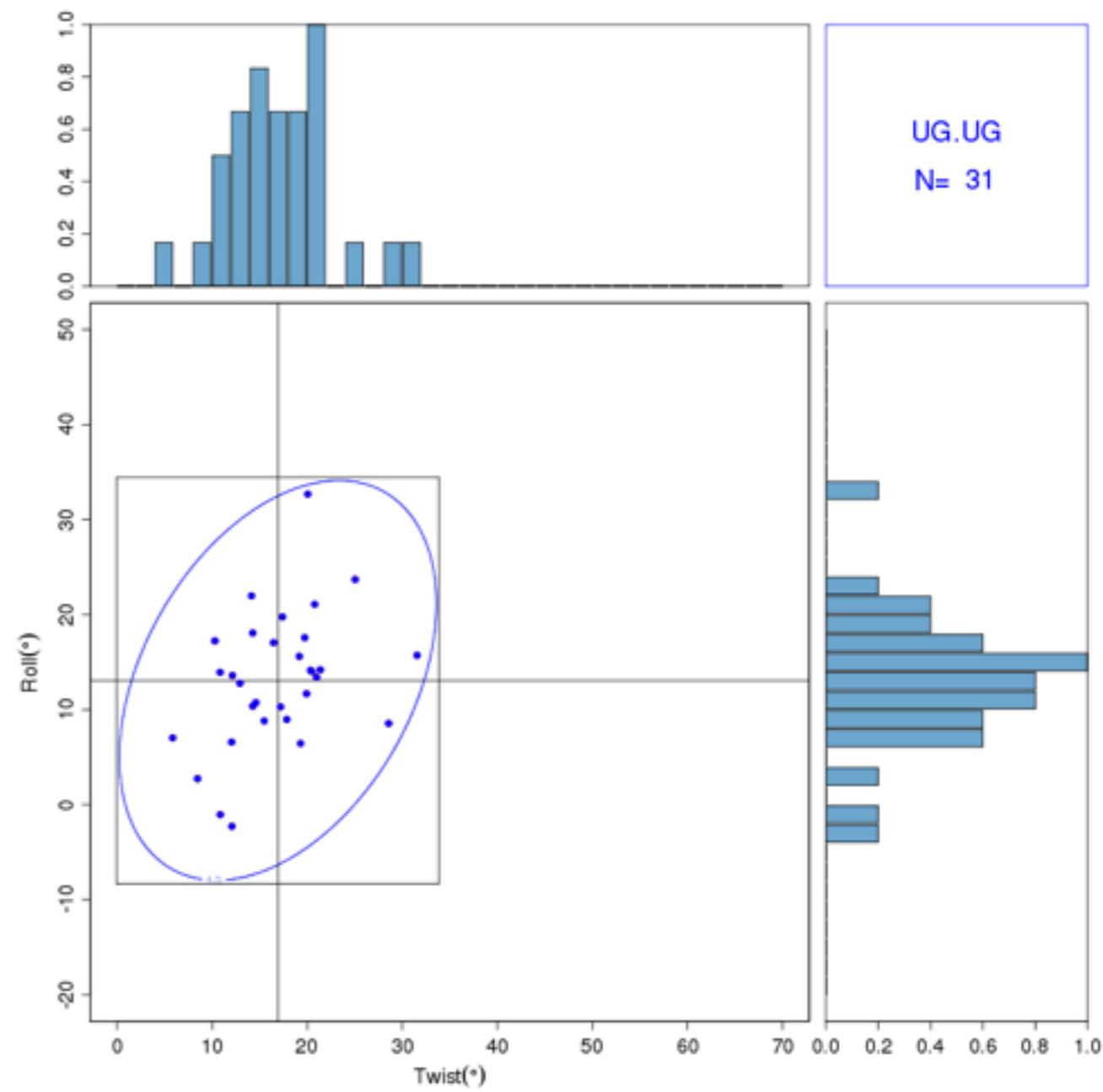
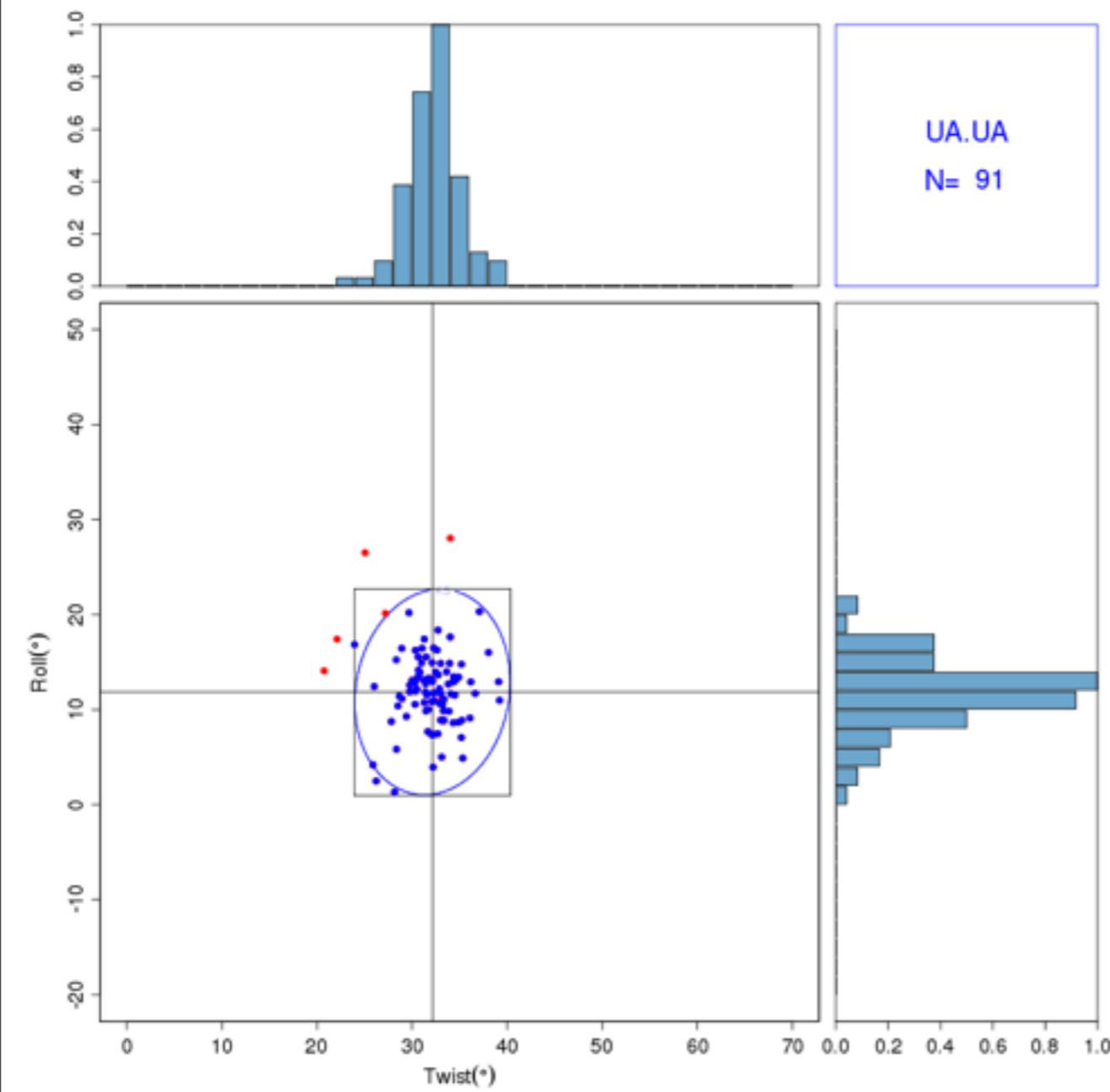
- From Base-pair step parameters, inverse covariance matrix and you get analog to force-constant matrix.
- With force constants you can make a simple spring model, your good ole Hooke's law in sixth dimension.

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

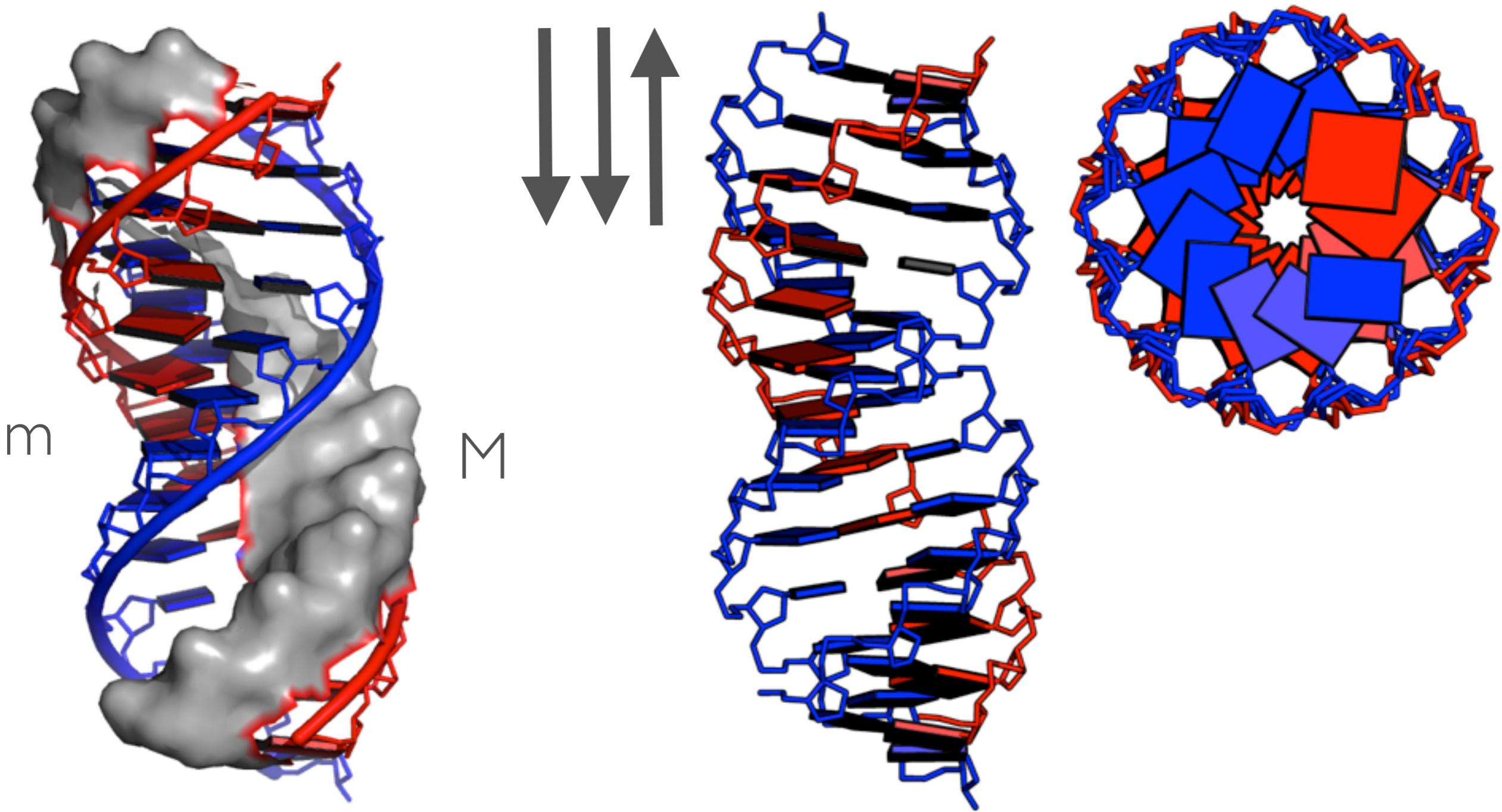
$$(\Delta x_i = x_i - x_{i0})$$

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

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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Nature Protocols, Department of Chemistry and Chemical Biology and BioMaPS Institute for Quantitative Biology, Rutgers-The State University of New Jersey, Piscataway, New Jersey 08854-8087, USA. 3dna.lu@gmail.com, **2008**, 3, 1213-1227

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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.