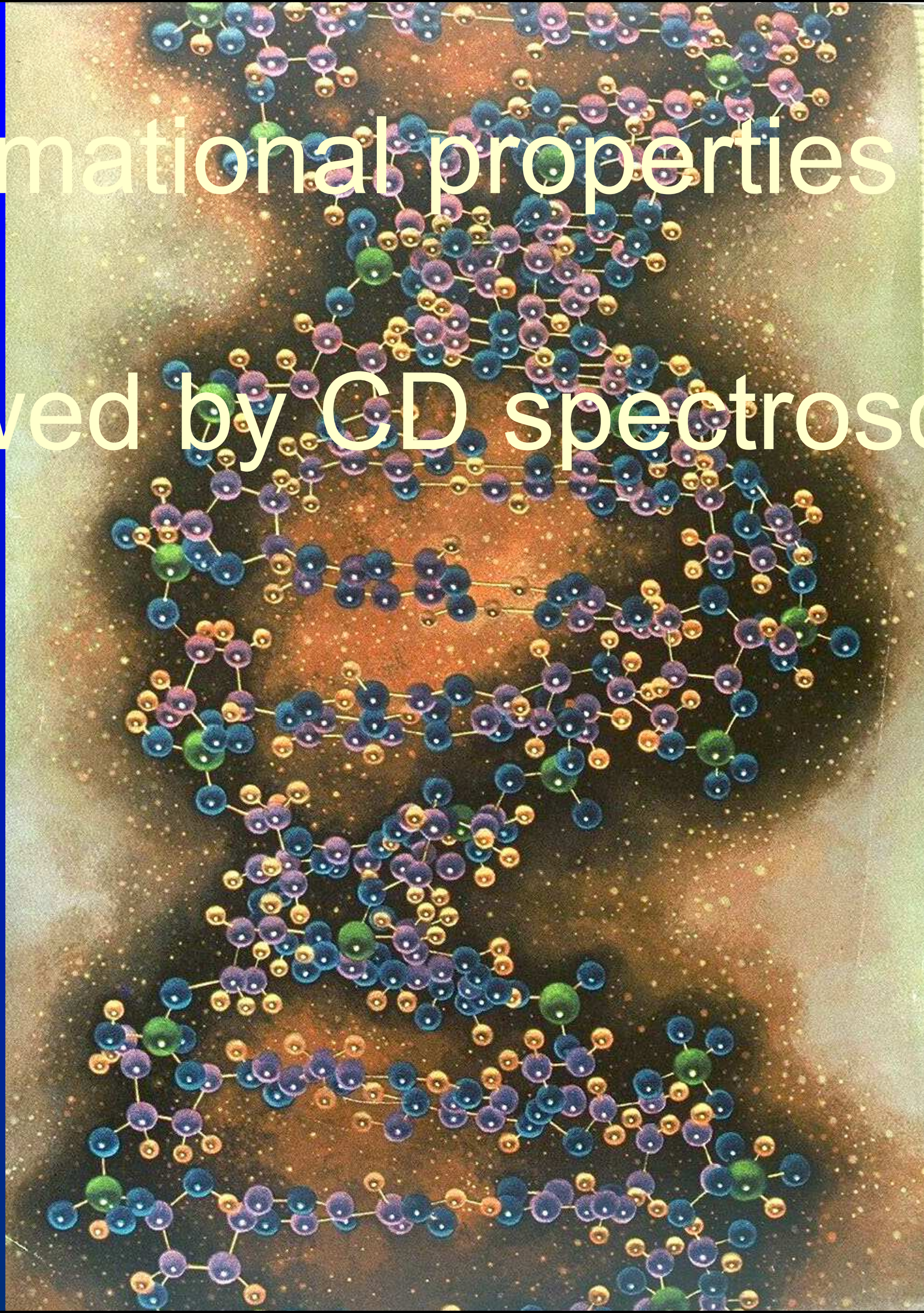
Conformational properties of DNA

viewed by CD spectroscopy



Laboratory of CD spectroscopy of nucleic acids

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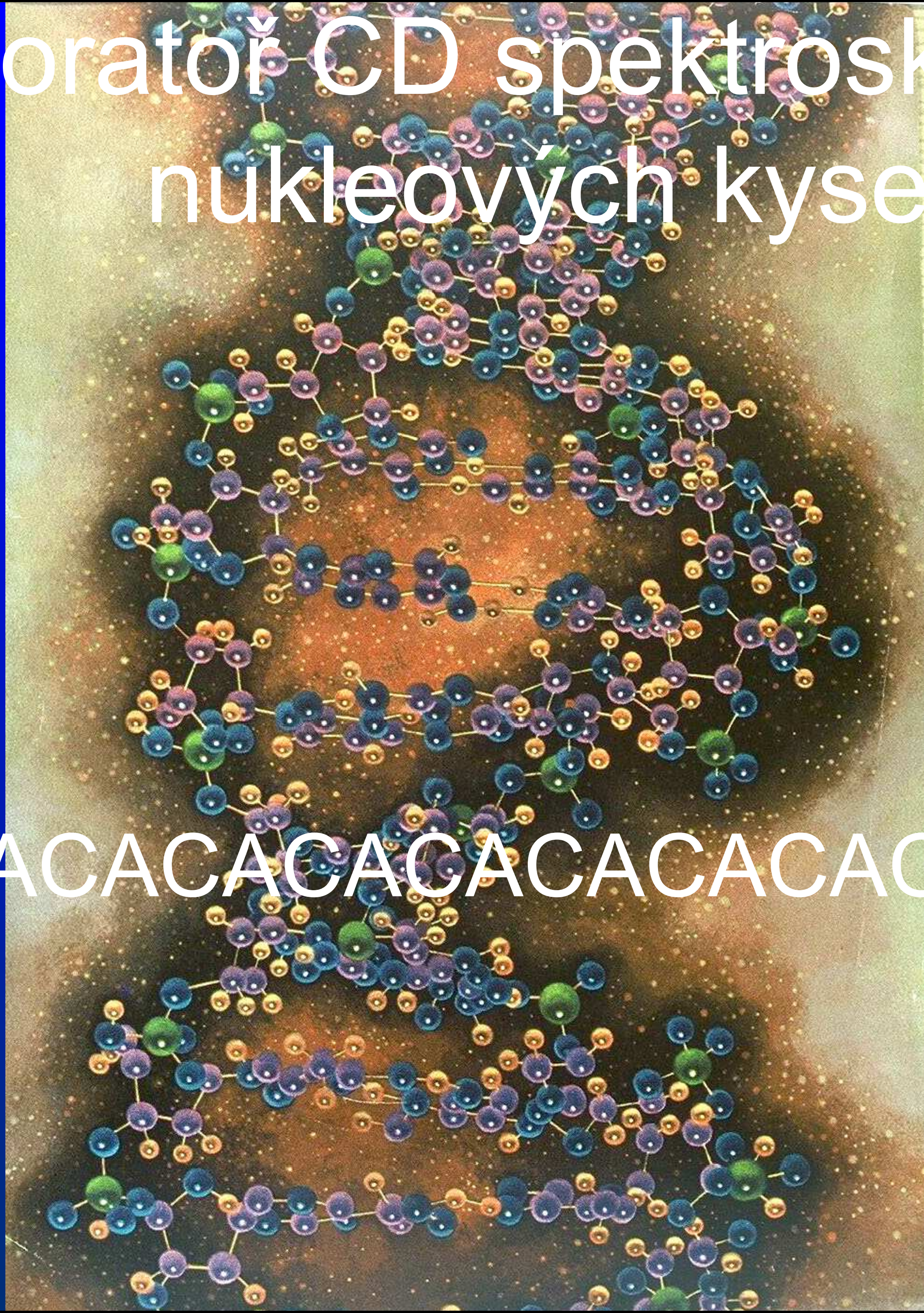
Institute of Biophysics
Academy of Sciences of the Czech Republic, v.v.i.
Brno

Laboratoř CD spektroskopie nukleových kyselin

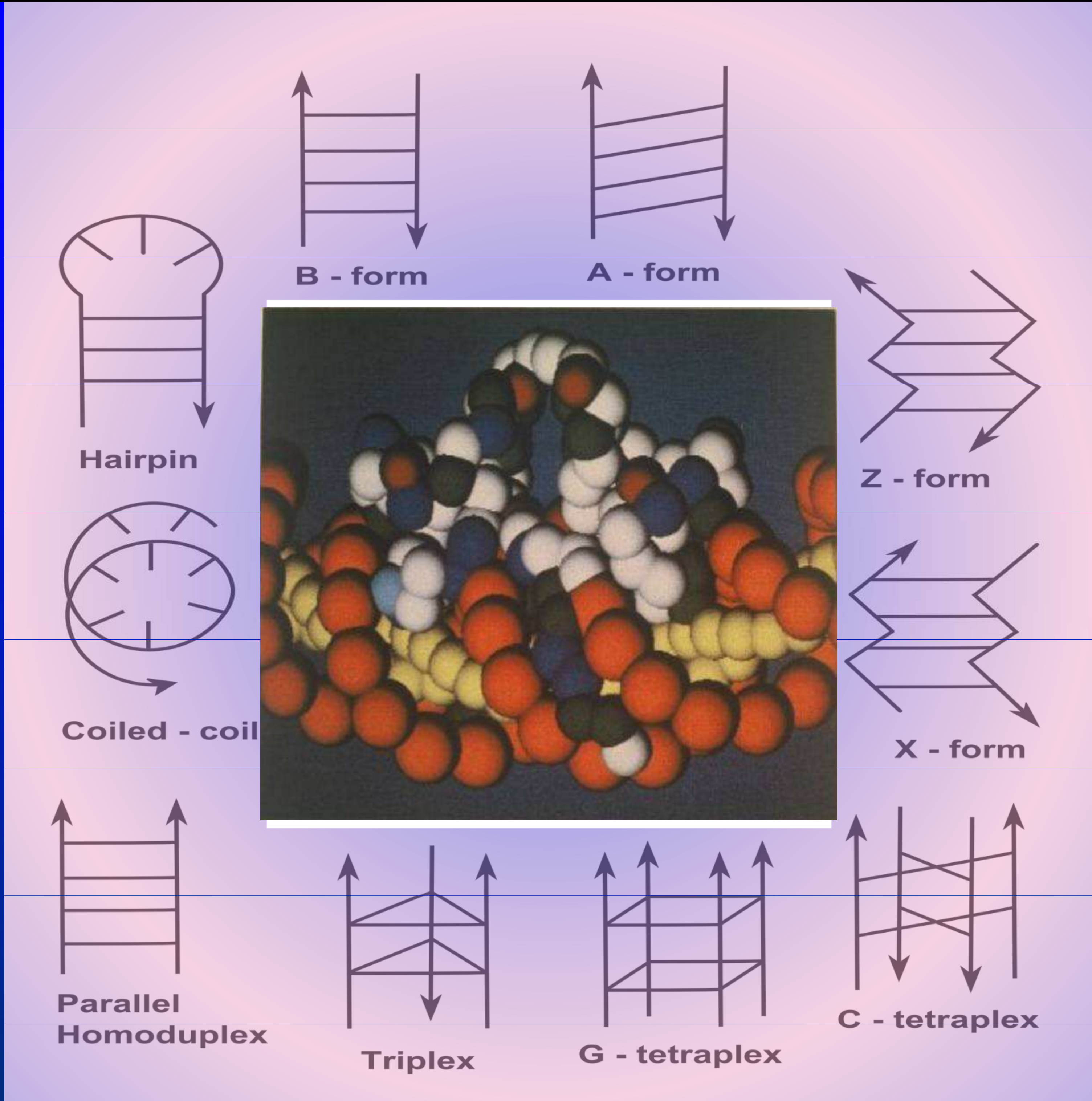


3.10^9

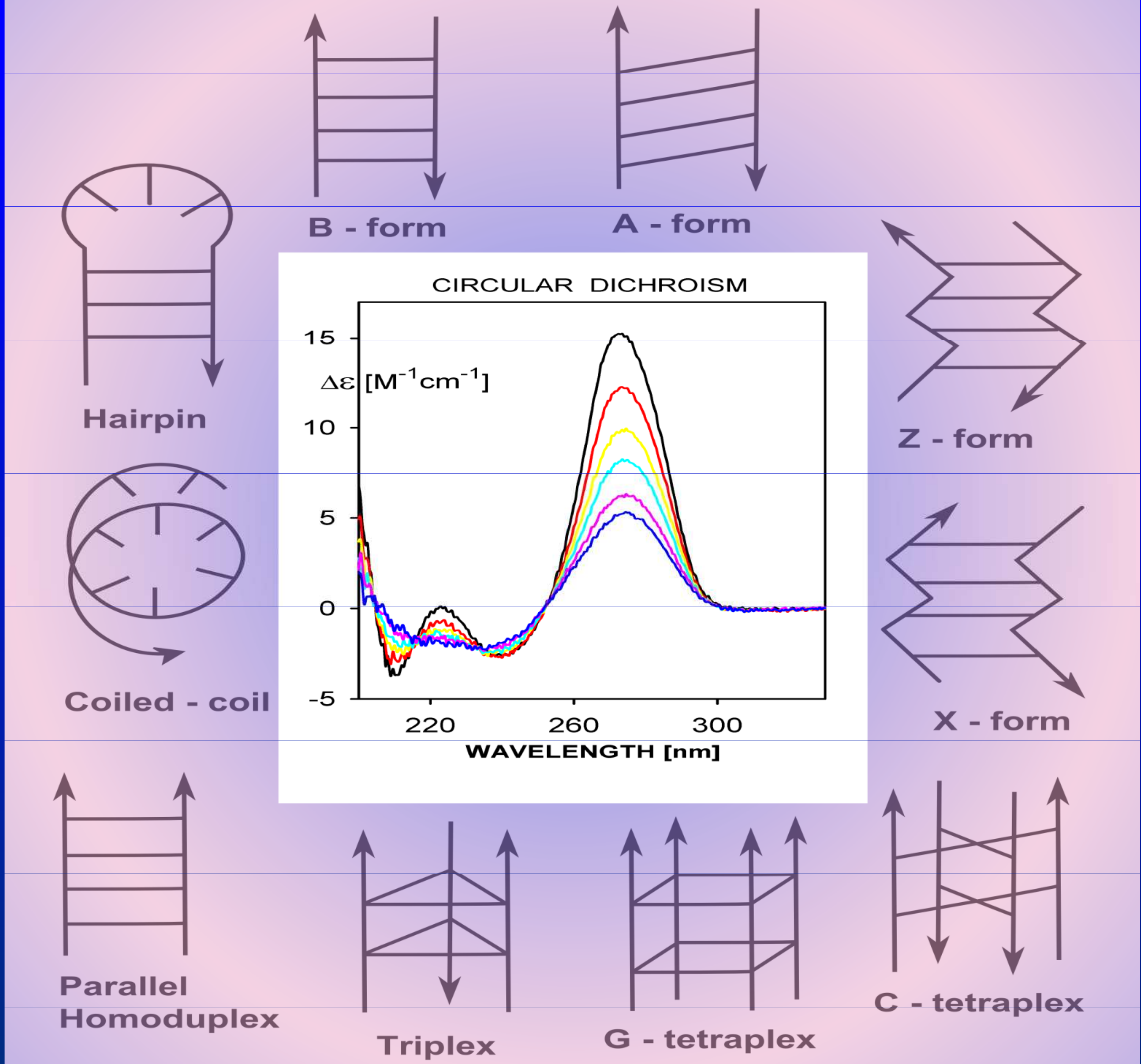
A C G T

< 2 %

ACACACACACACACACACACACACACACACAC

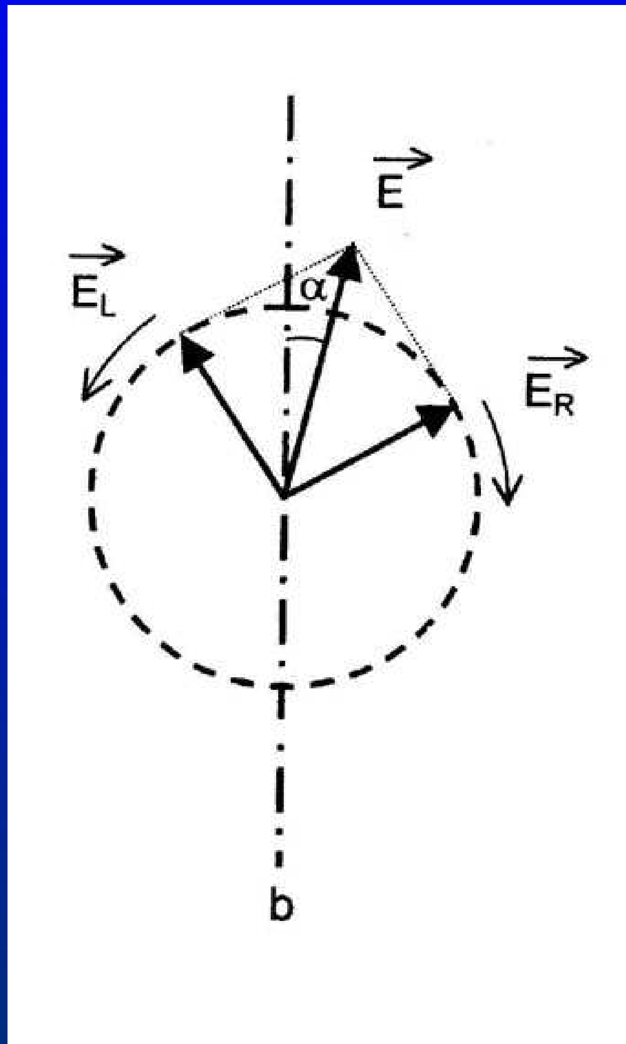


B - form
A - form
Hairpin
Z - form
Coiled - coil
X - form
Parallel
Homoduplex
Triplex
G - tetraplex
C - tetraplex


B - form
A - form
Hairpin
Z - form
Coiled - coil
X - form
CIRCULAR DICHROISM
Δε [M⁻¹cm⁻¹]
15
10
5
0
-5
220
260
300
WAVELENGTH [nm]
Parallel
Homoduplex
Triplex
G - tetraplex
C - tetraplex

Cirkulární dichroismus a optická aktivita biopolymerů

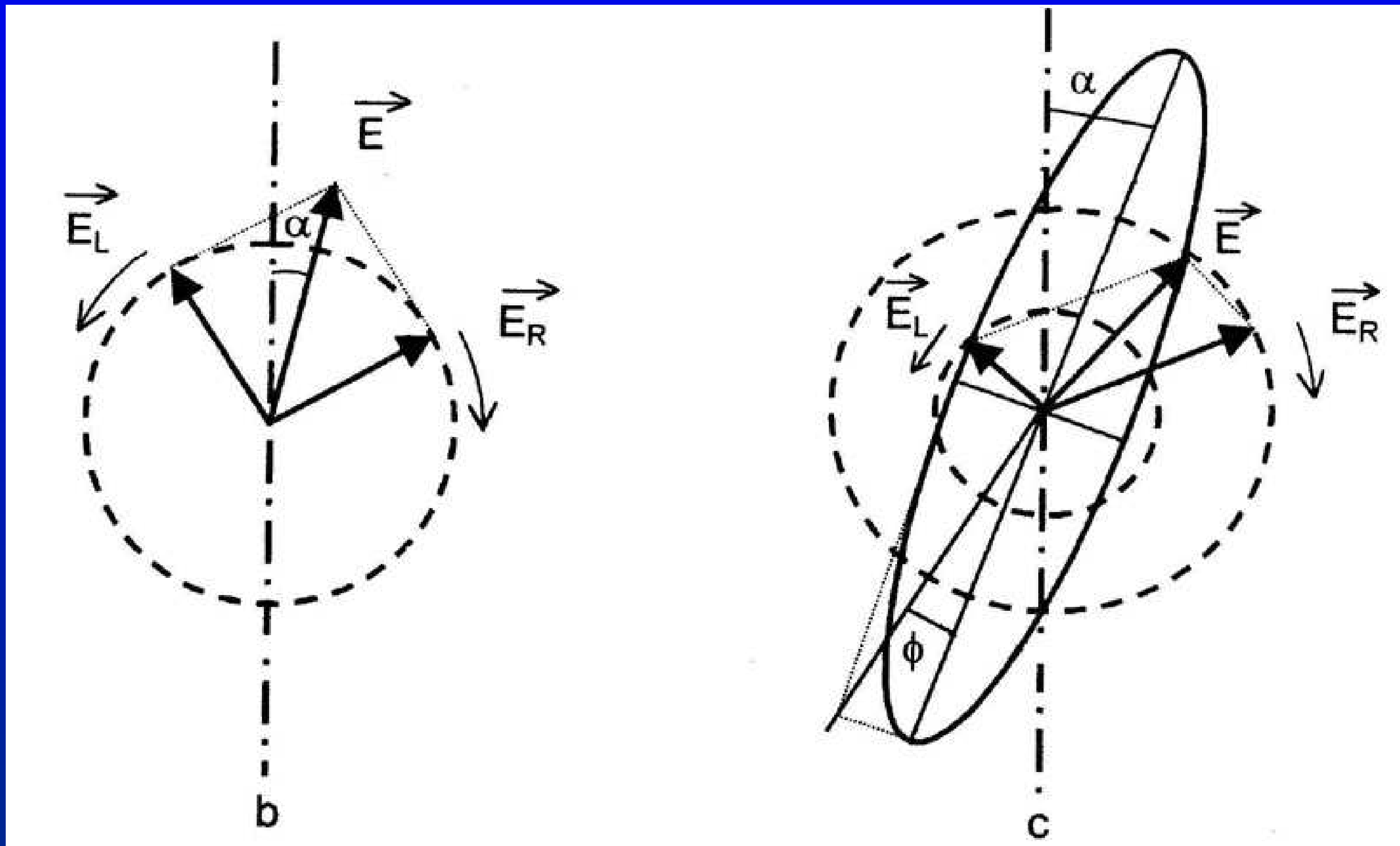
) optická aktivita – chirální látky (aminokyseliny, cukry) úhel stočení roviny polarizovaného světla, ORD



Cirkulární dichroismus a optická aktivita biopolymerů

) optická aktivita – chirální látky (aminokyseliny, cukry) úhel stočení roviny polarizovaného světla, ORD

) CD – princip, veličiny, elipticita, ΔA, Δε, vztah mezi ORD a CD



Elipticita **φ** [ψ] $\mathrm{tg}\,\varphi = b/a = \varepsilon_L - \varepsilon_{R/}\,\varepsilon_L + \varepsilon_R$

Cirkulární dichroismus **Δε** $\Delta\varepsilon = \varepsilon_L - \varepsilon_R = \Delta A/lc$

Cicular dichroism

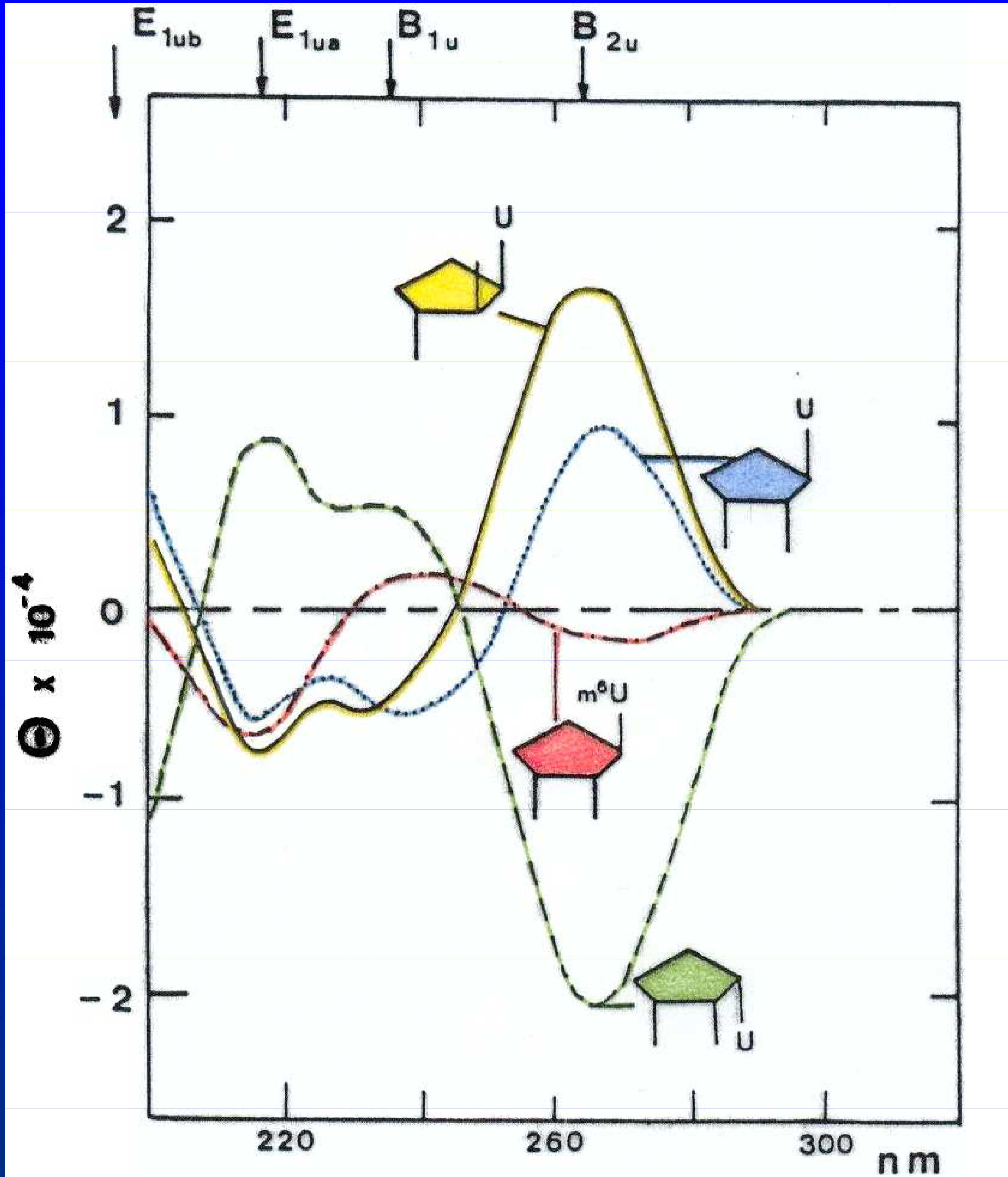
ABSORPTION

+ **CD**

CHIRALITY

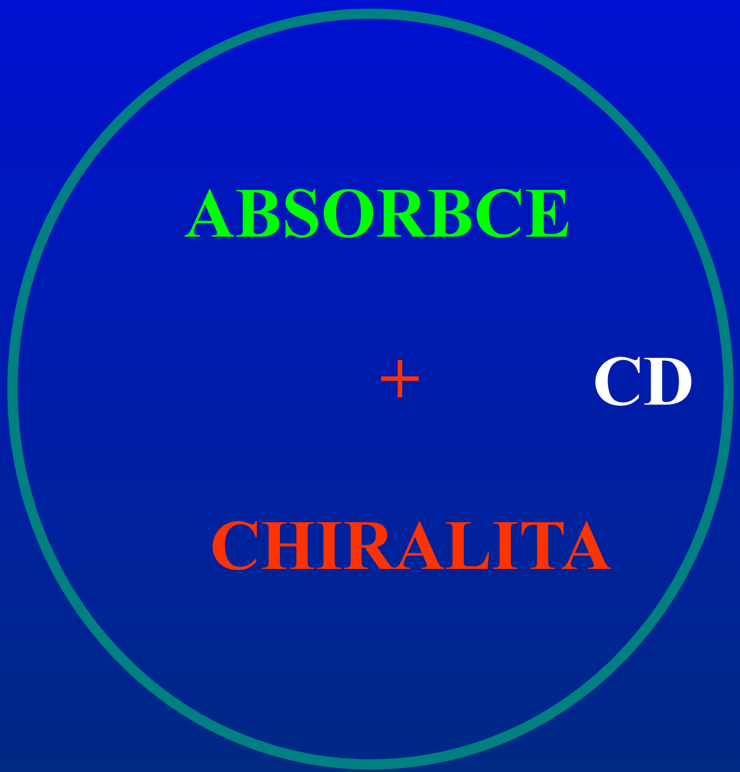
BASE

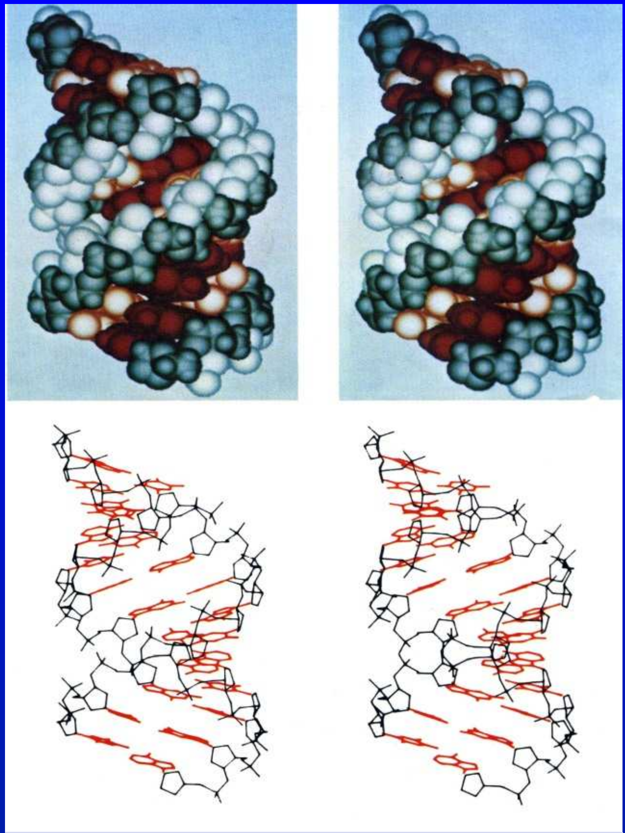
* CUGAR



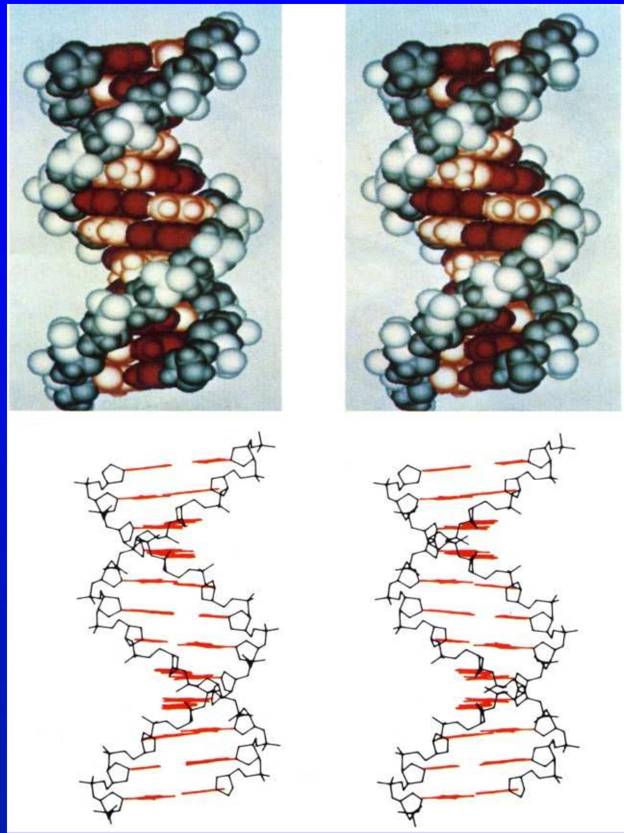
E_{1ub}
E_{1ua}
B_{1u}
B_{2u}
2
1
0
−1
−2
Θ x 10^{-4}
U
U
m^6U
U
220
260
300
nm

Podmínky vzniku CD

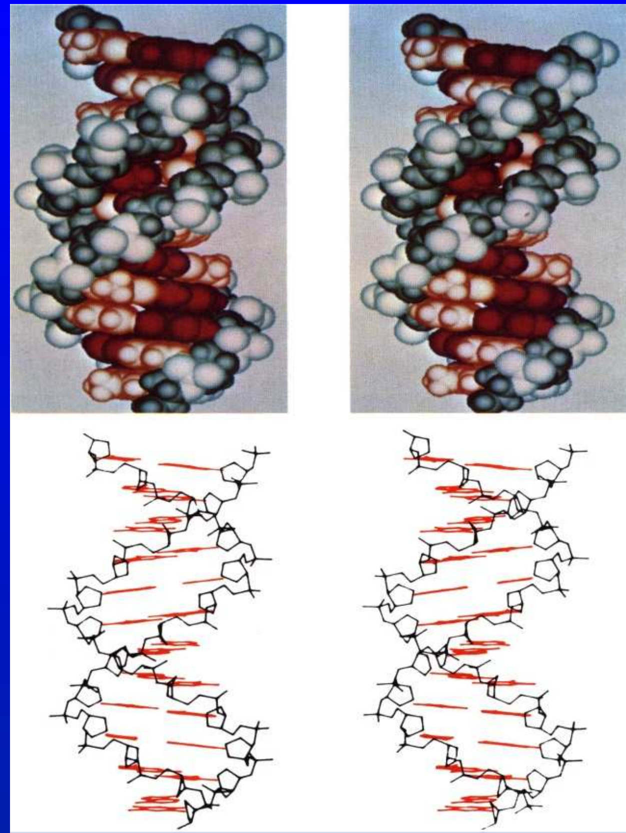




A



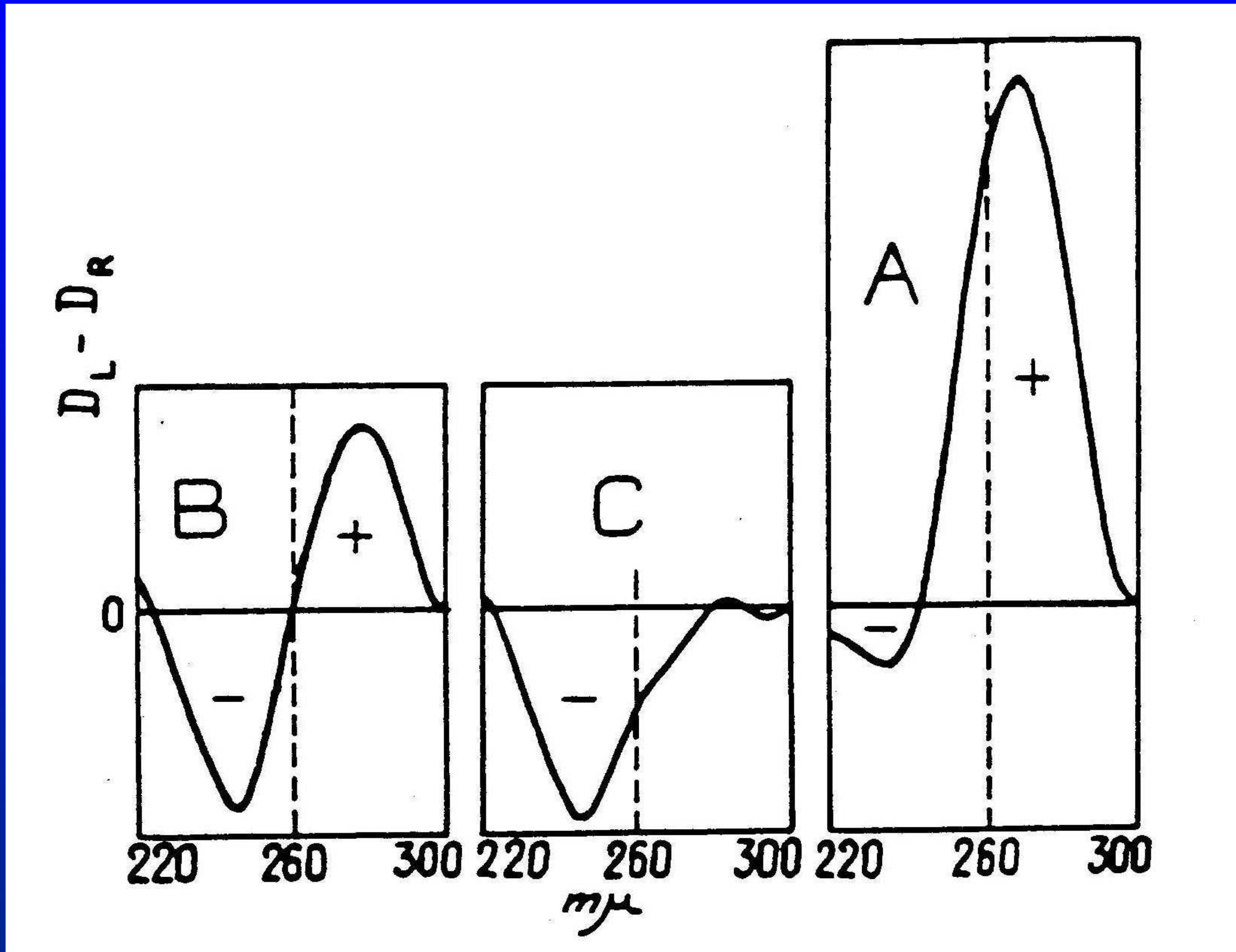
B



C,D,T

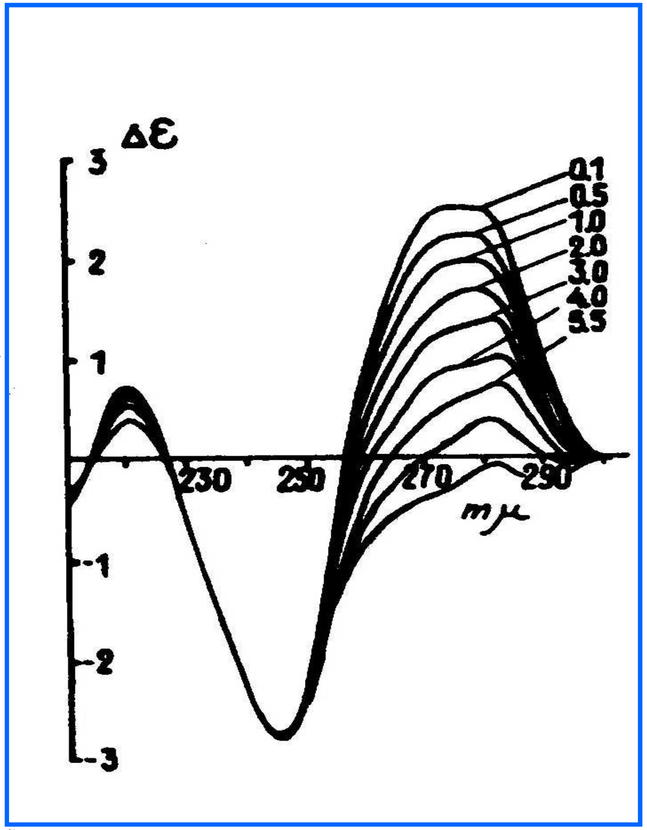
Wilkins+ Franklin

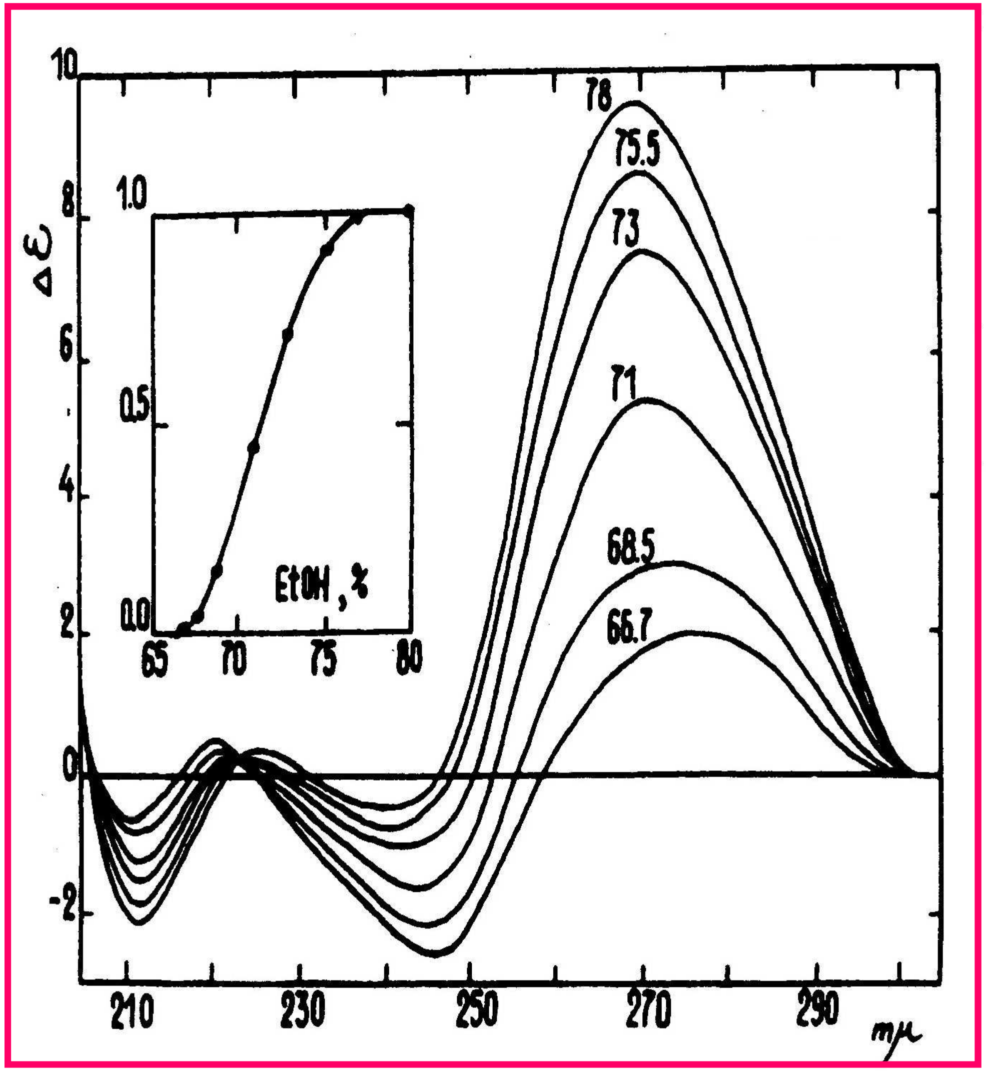
Tunis-Schneider, M.J.B. + Maestre, M.F.



Structural changes

Non-cooperative changes within the same structure

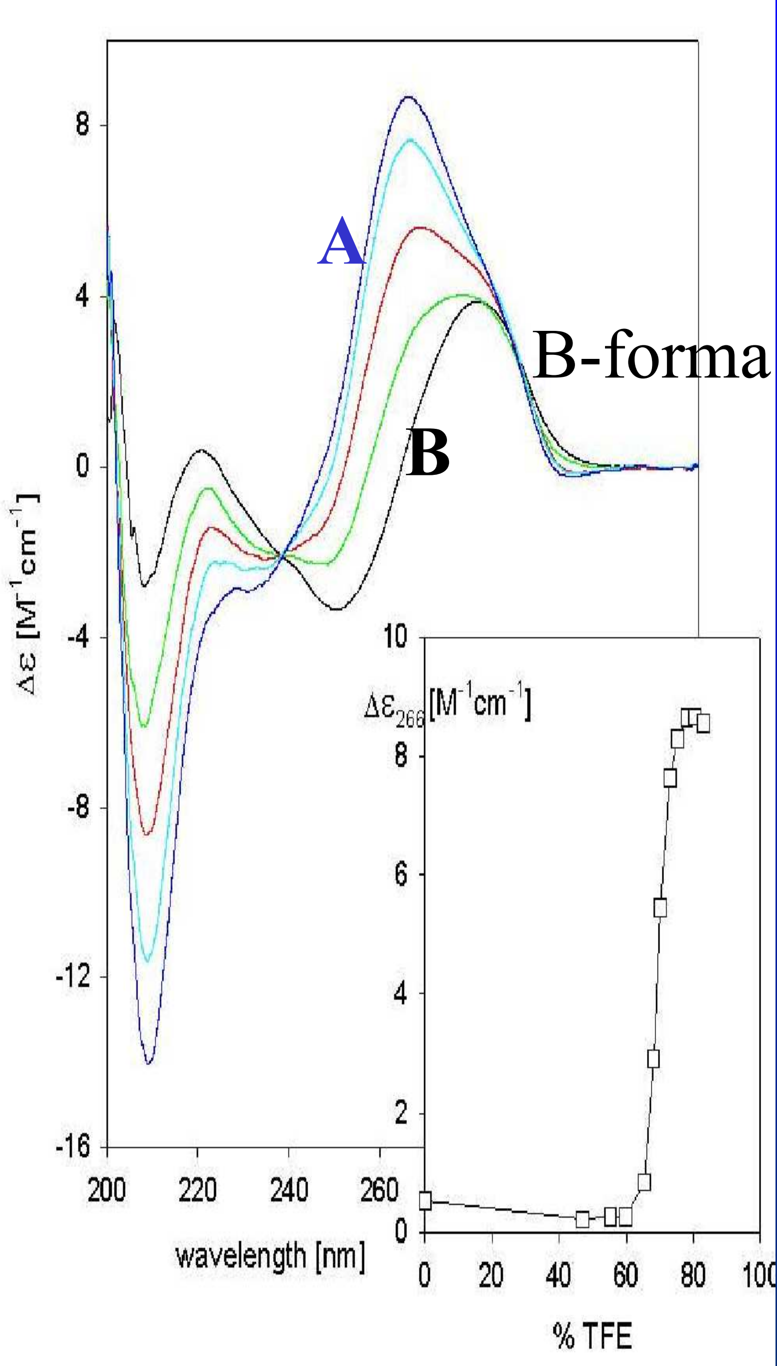


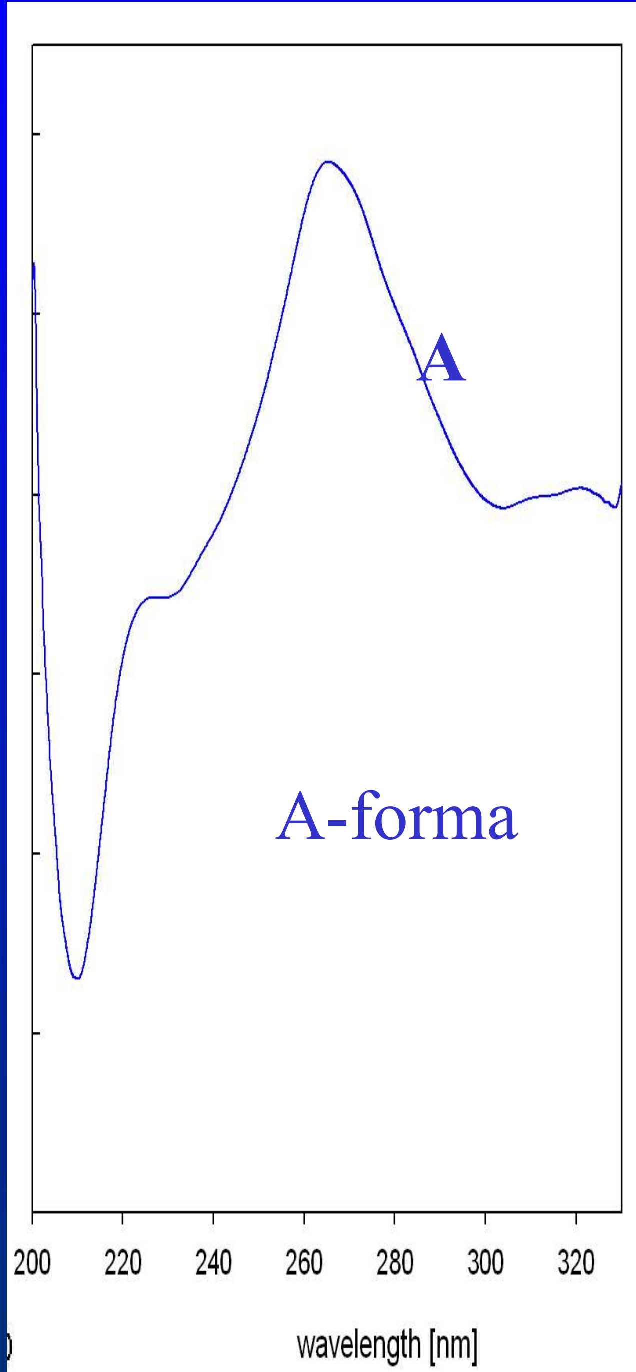


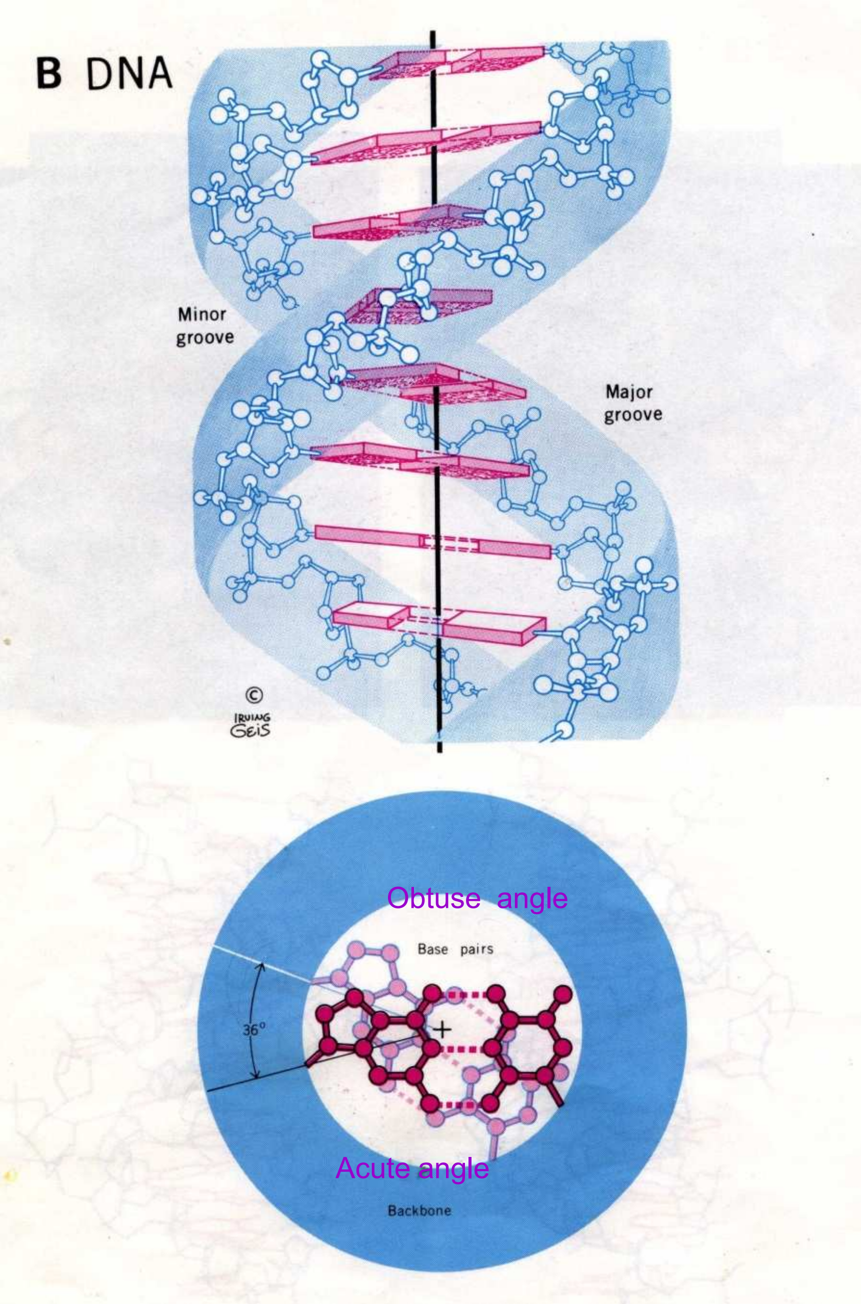
Cooperative changes between discreste structures

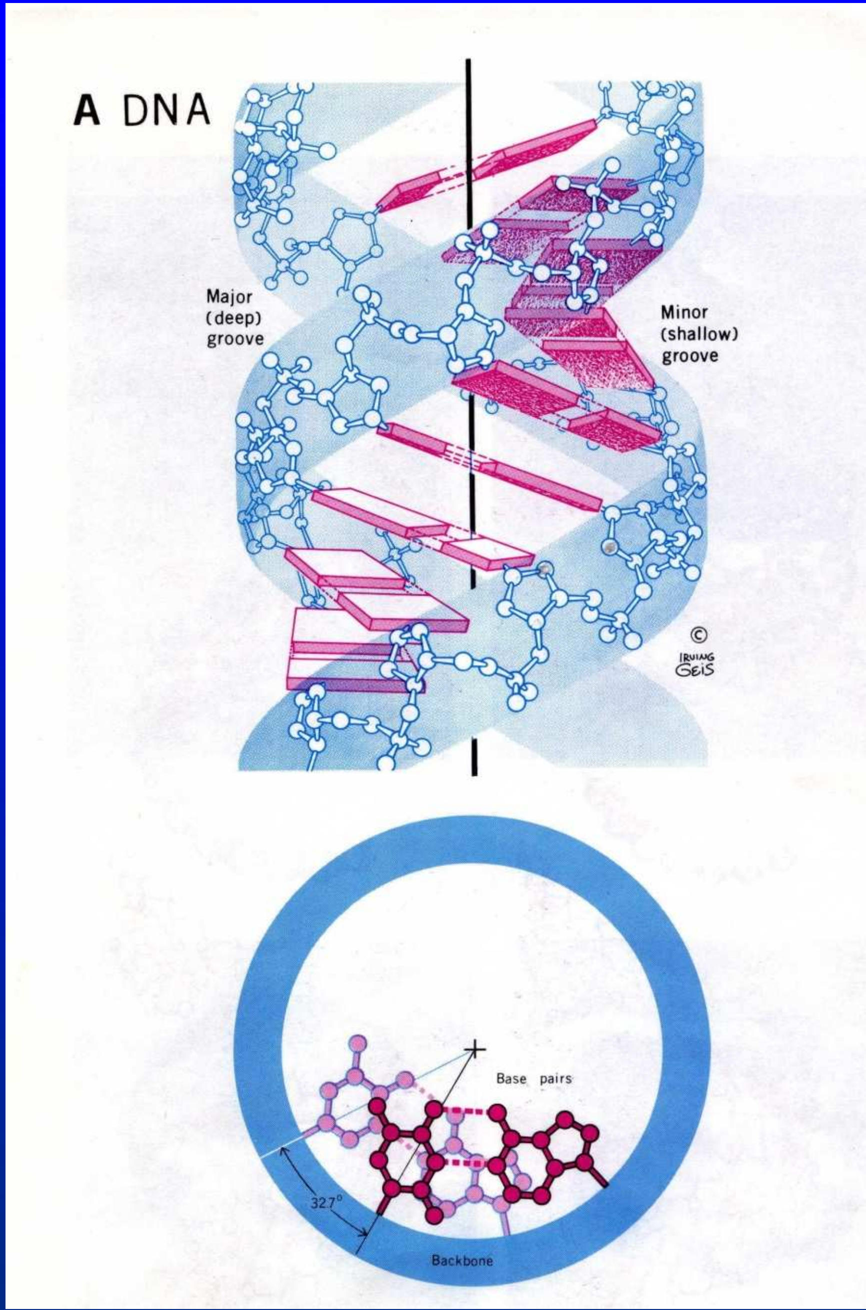
B-A DNA transition

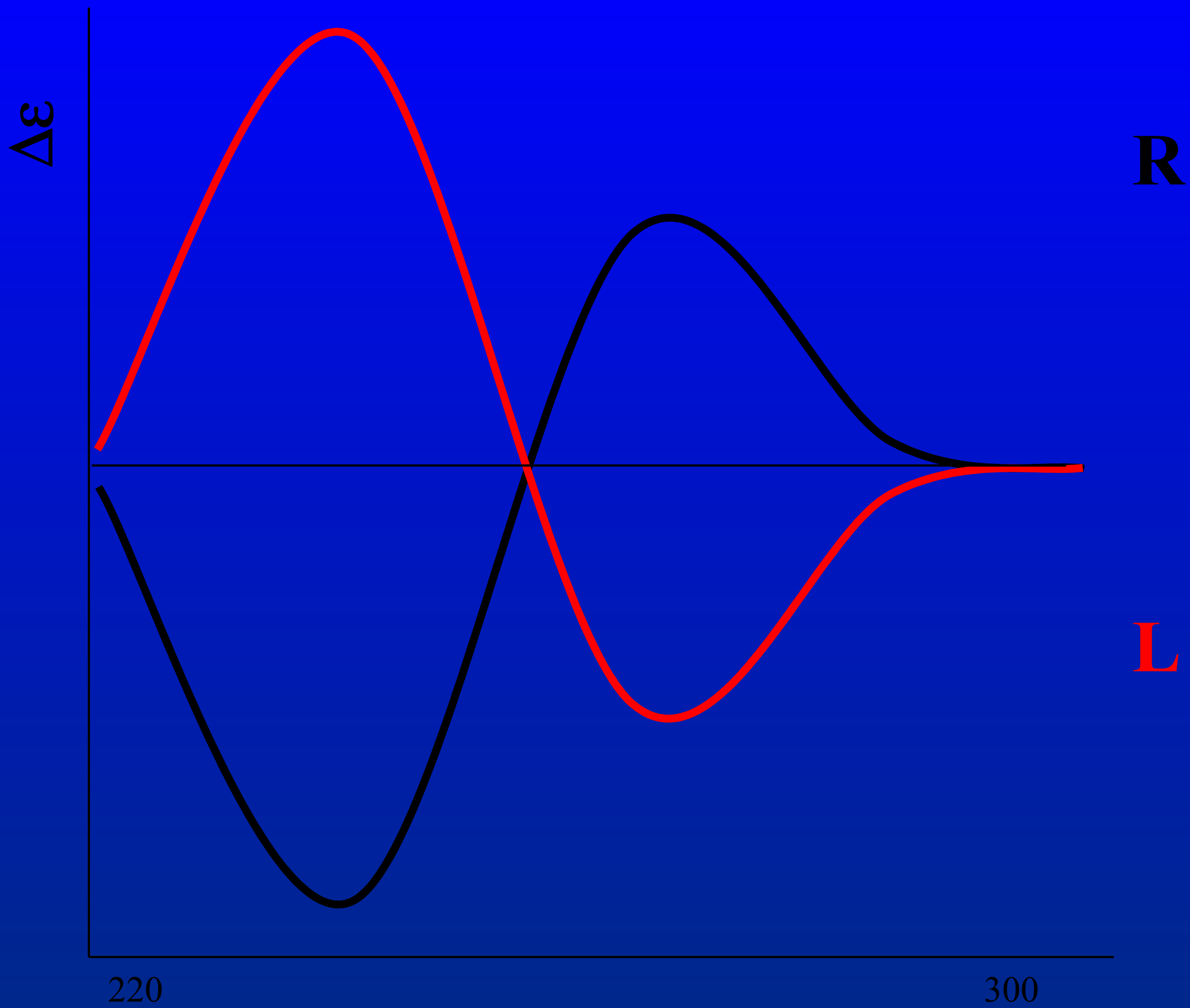
A -forma of RNA



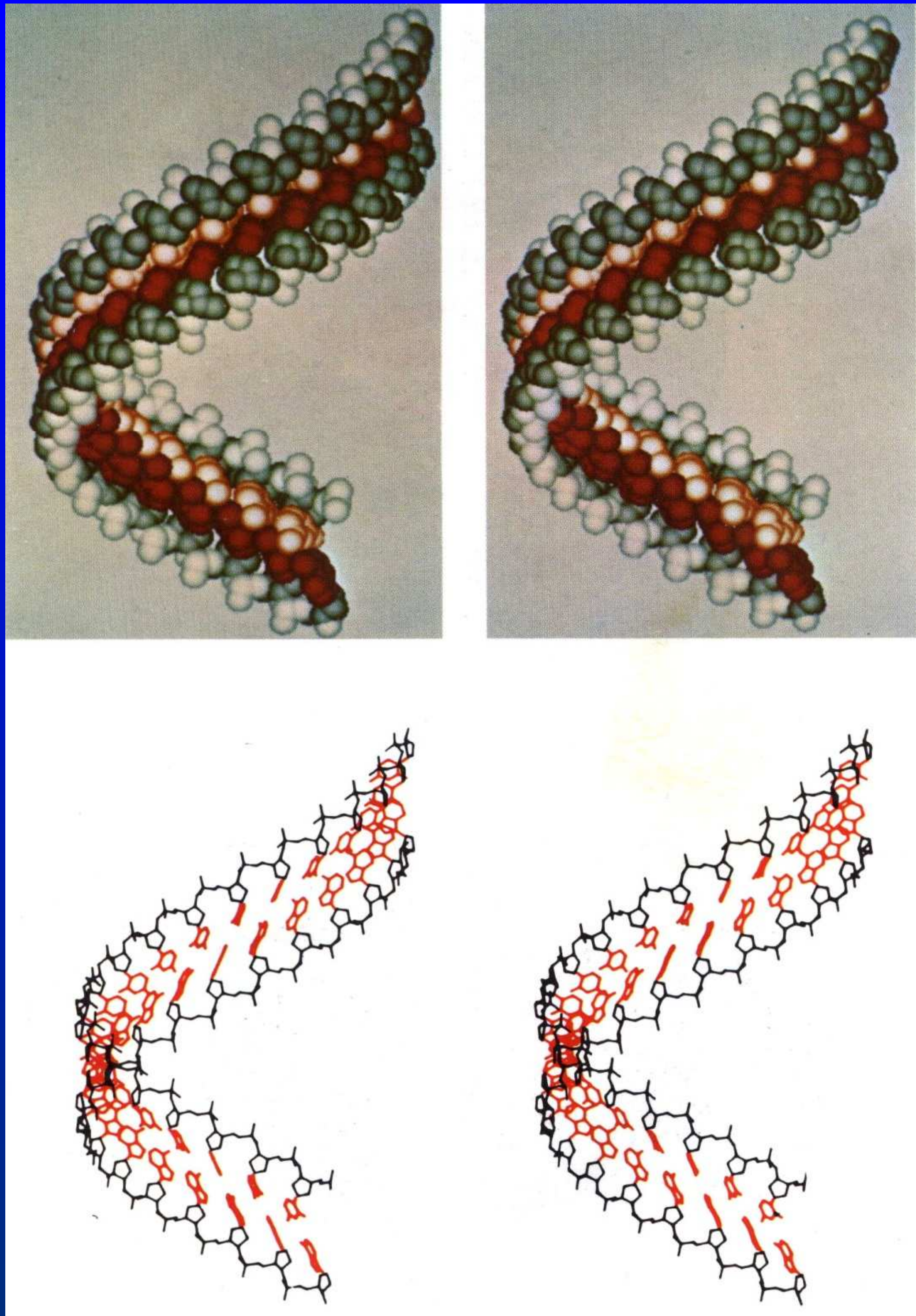



B DNA
Minor groove
Major groove
© IRVING GEIS
Obtuse angle
Base pairs
36°
Acute angle
Backbone

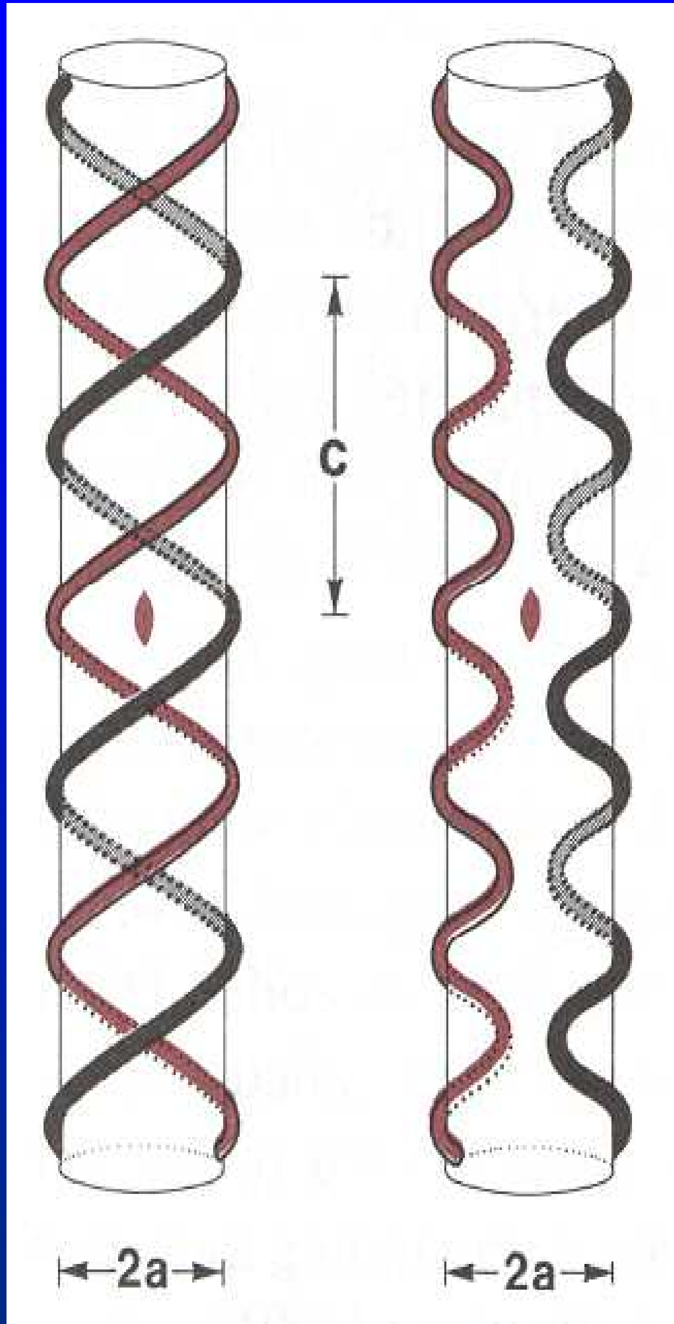

A DNA
Major (deep) groove
Minor (shallow) groove
© IRVING GEIS
Base pairs
32.7°
Backbone

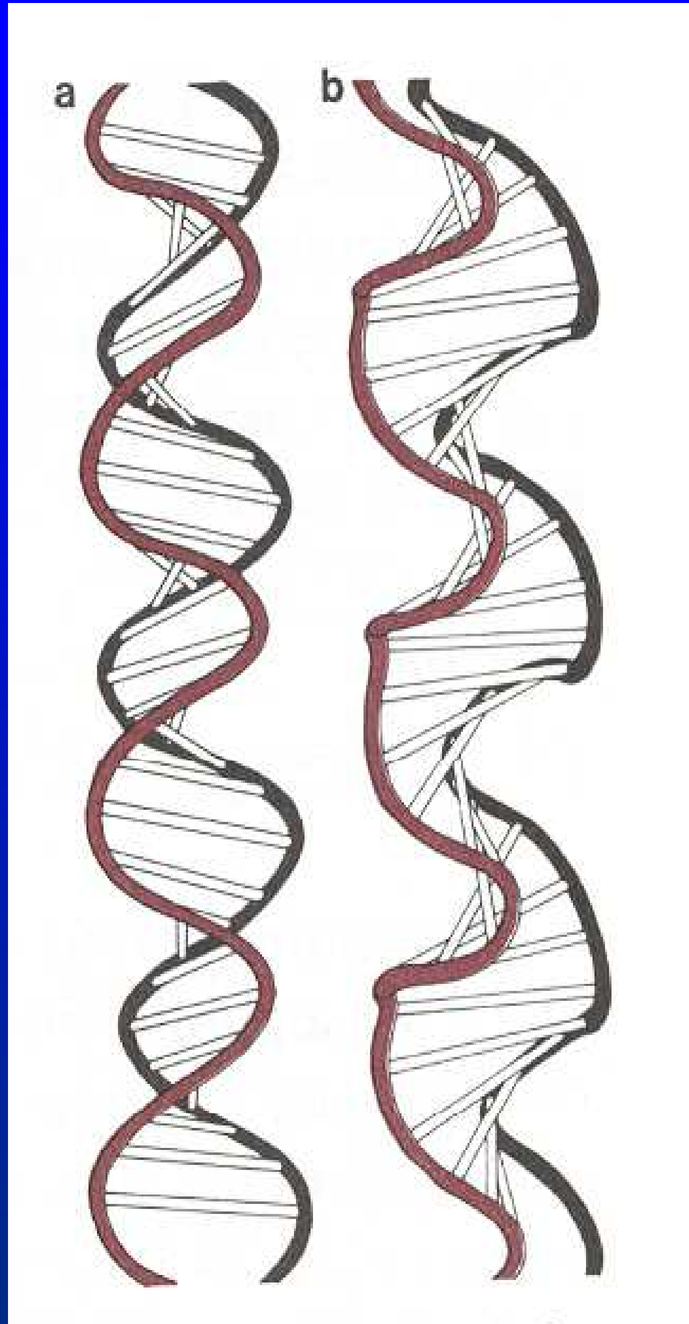


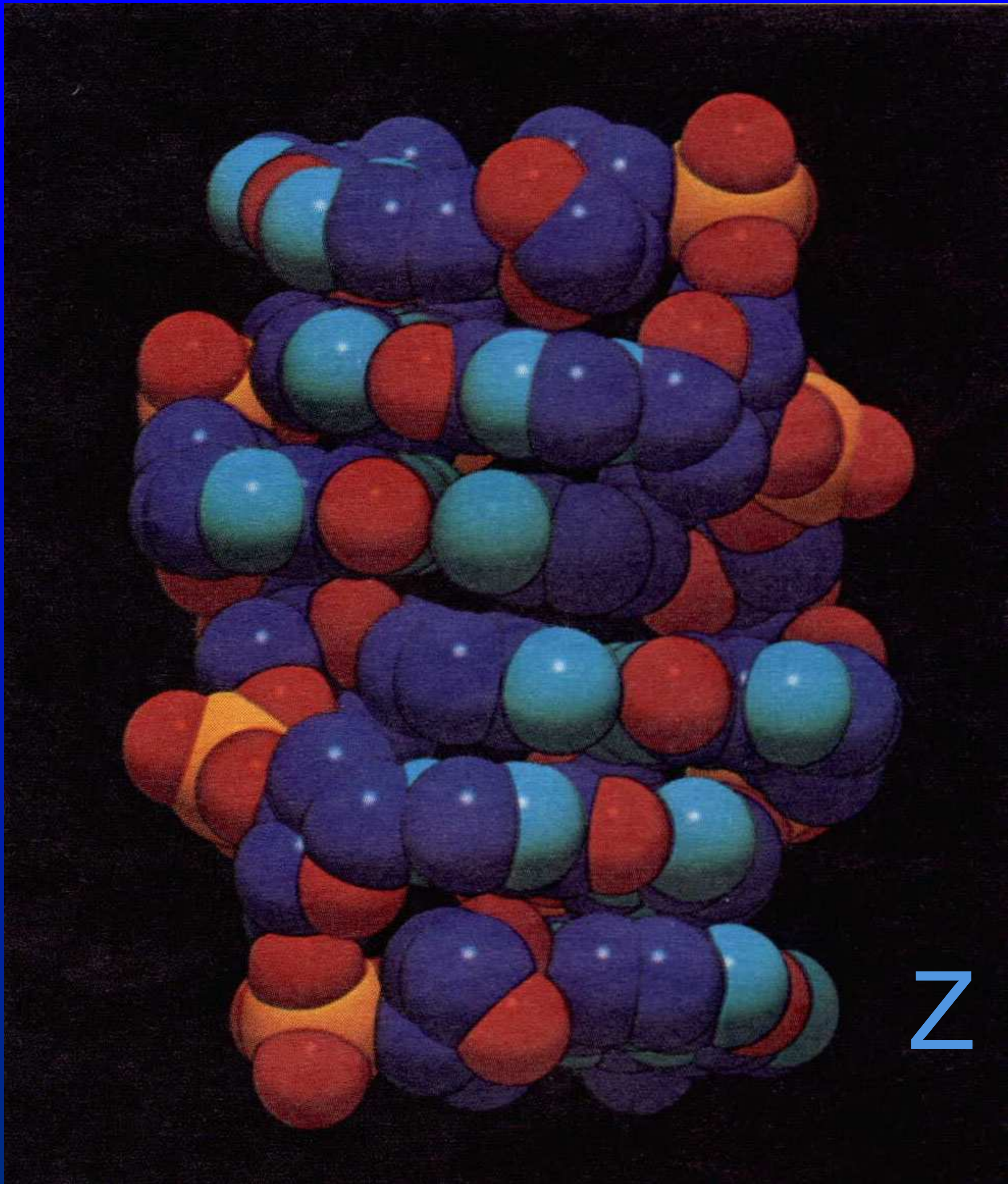
Δε
R
L
220
300

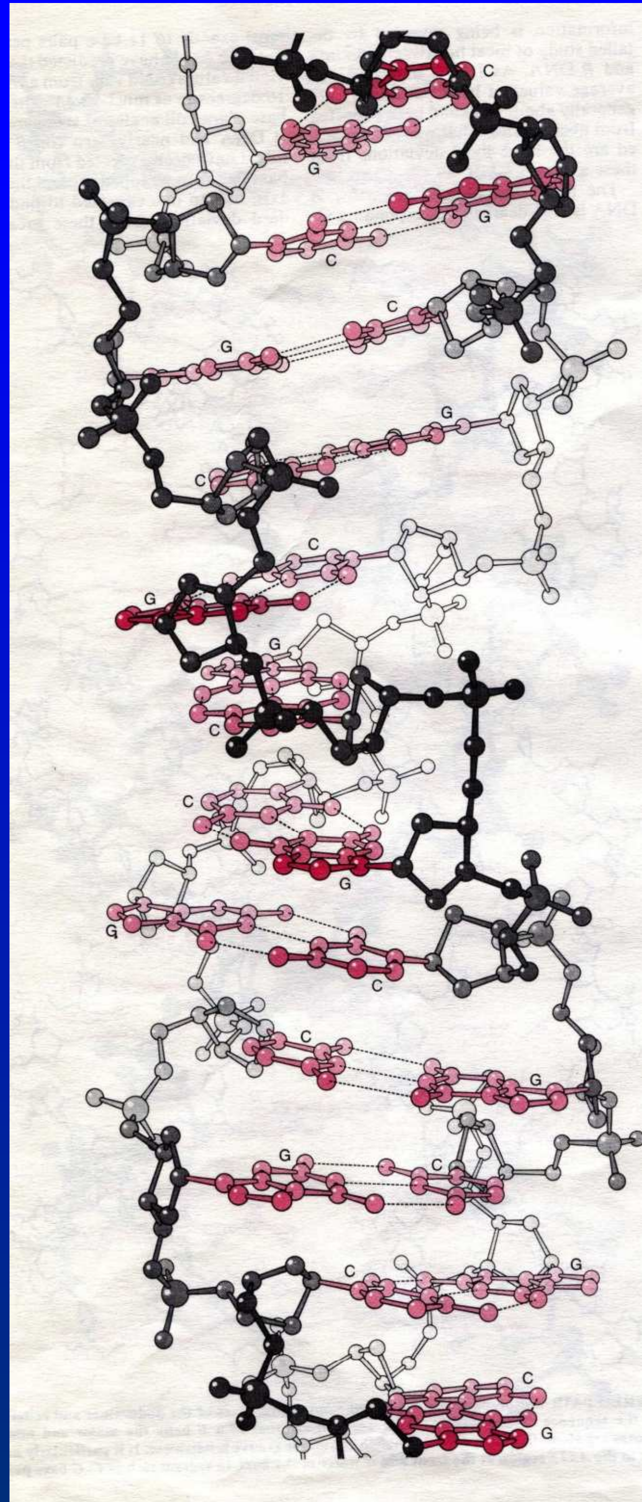


Vilma Olson

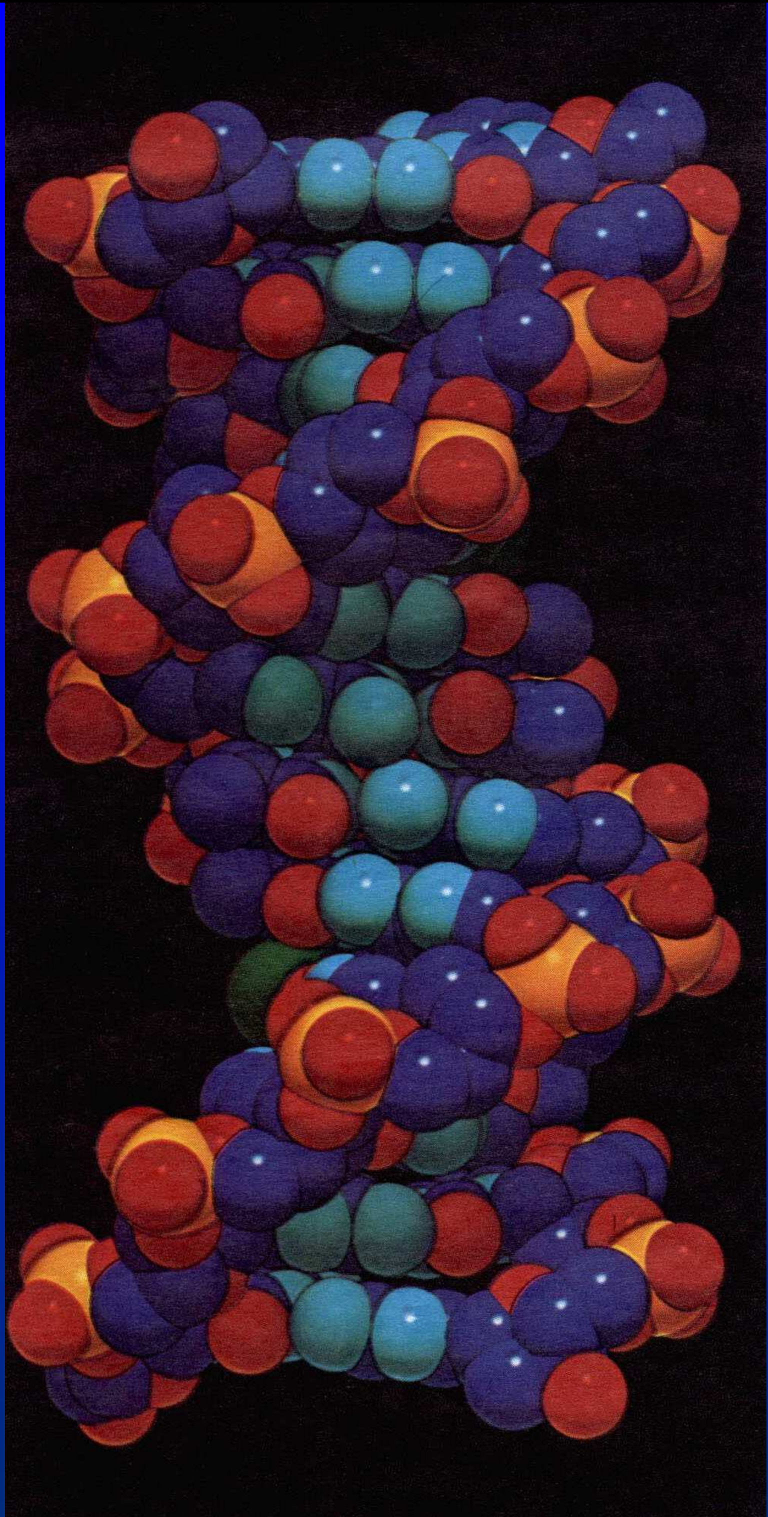

c
2a
2a


a
b

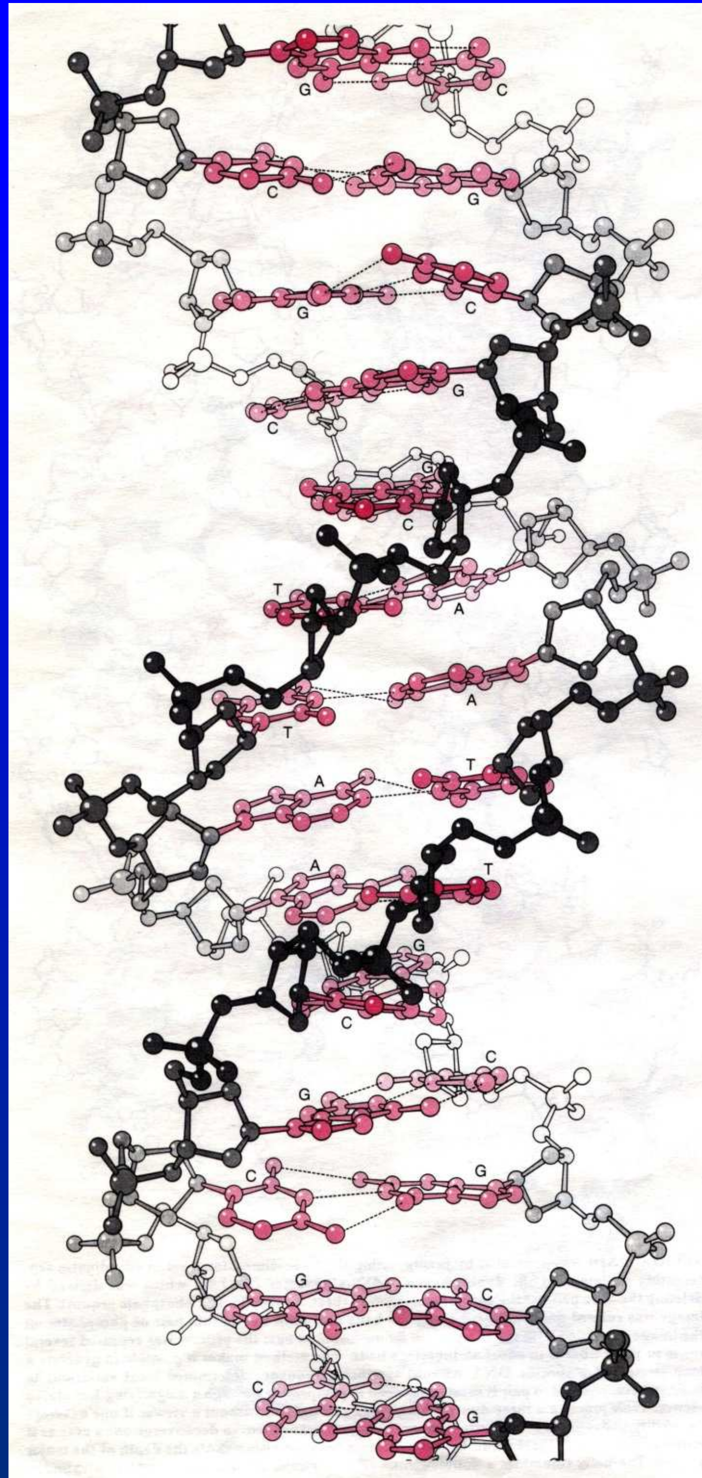


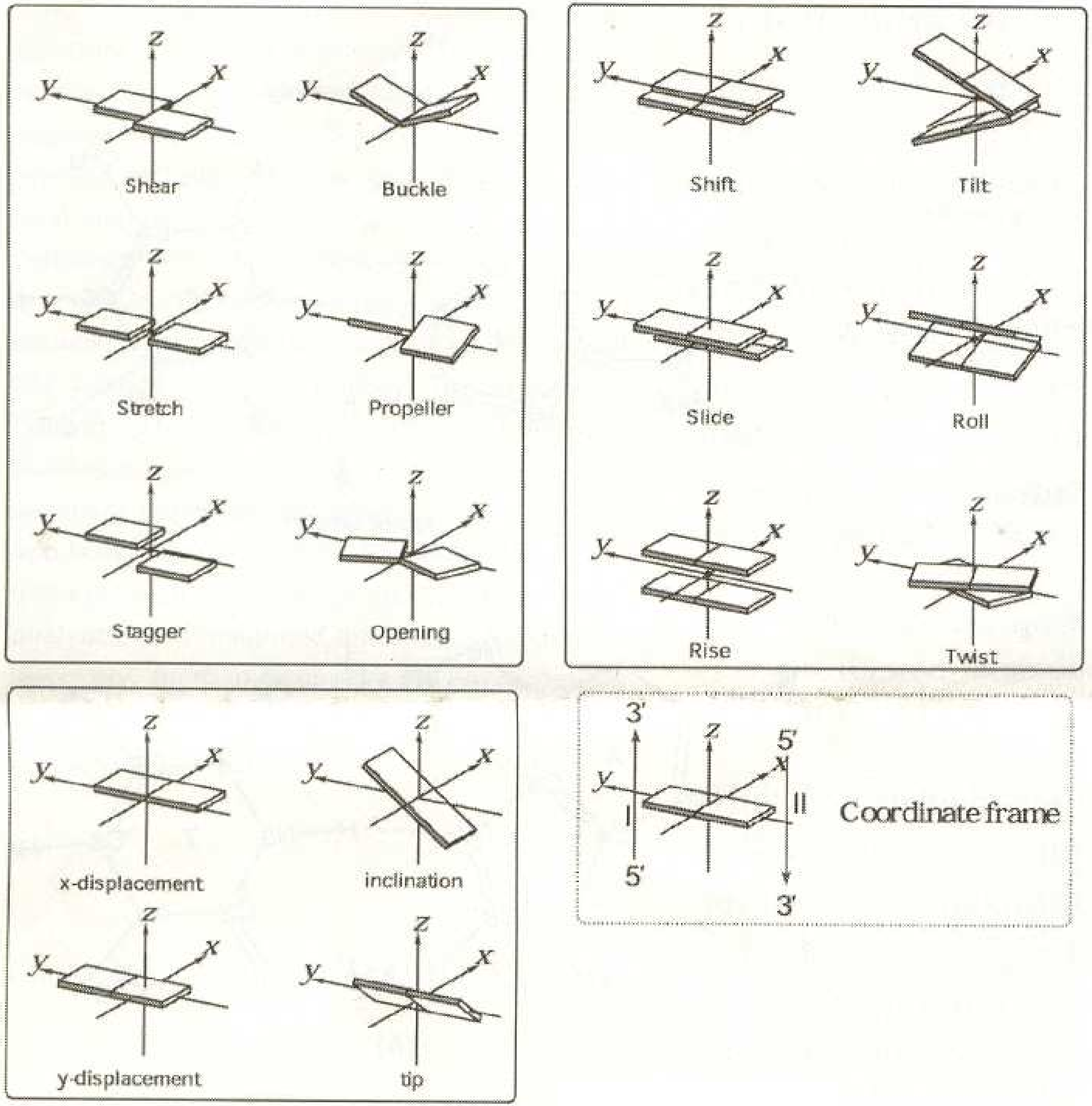


A. Rich MIT, Dickerson CalTech

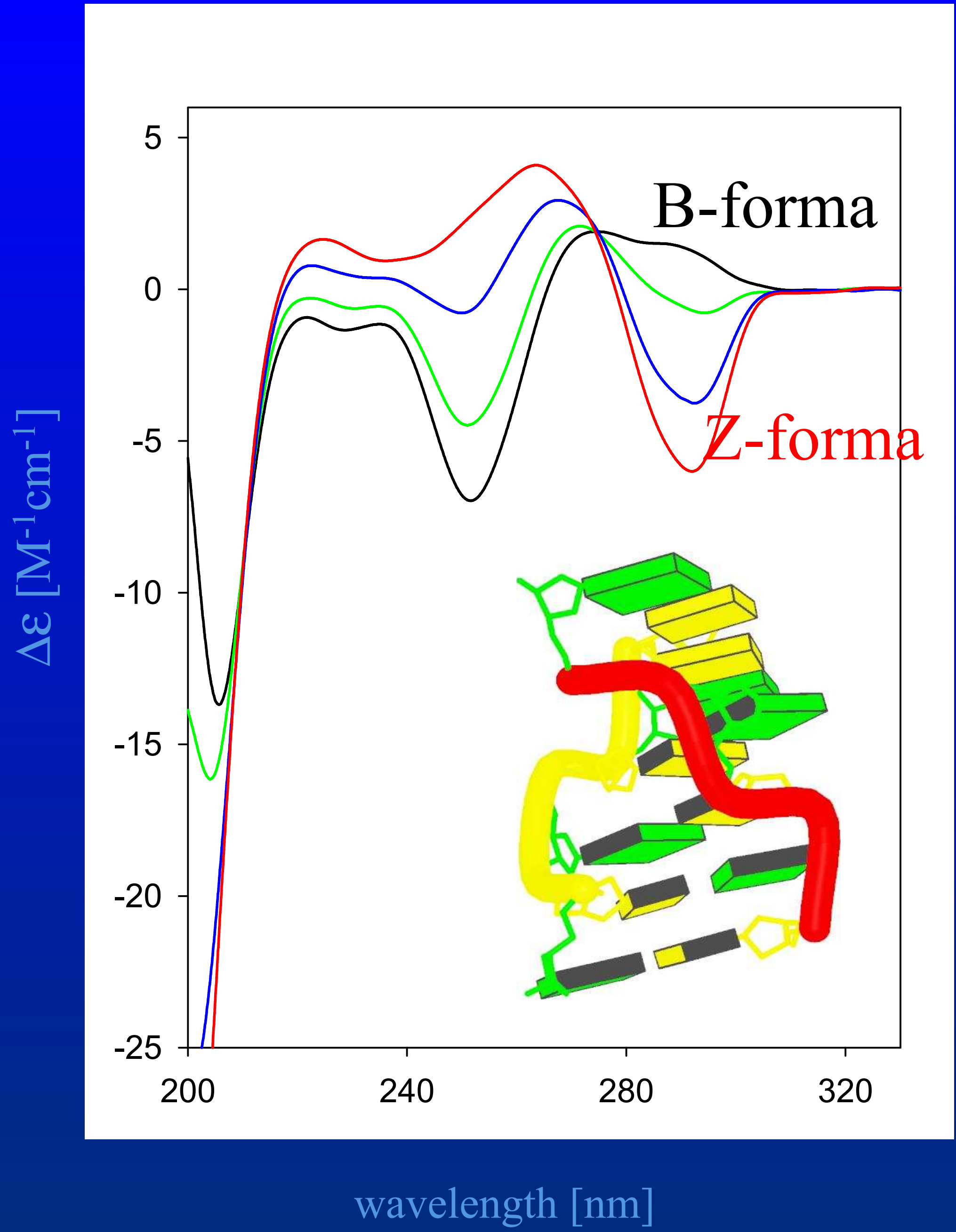


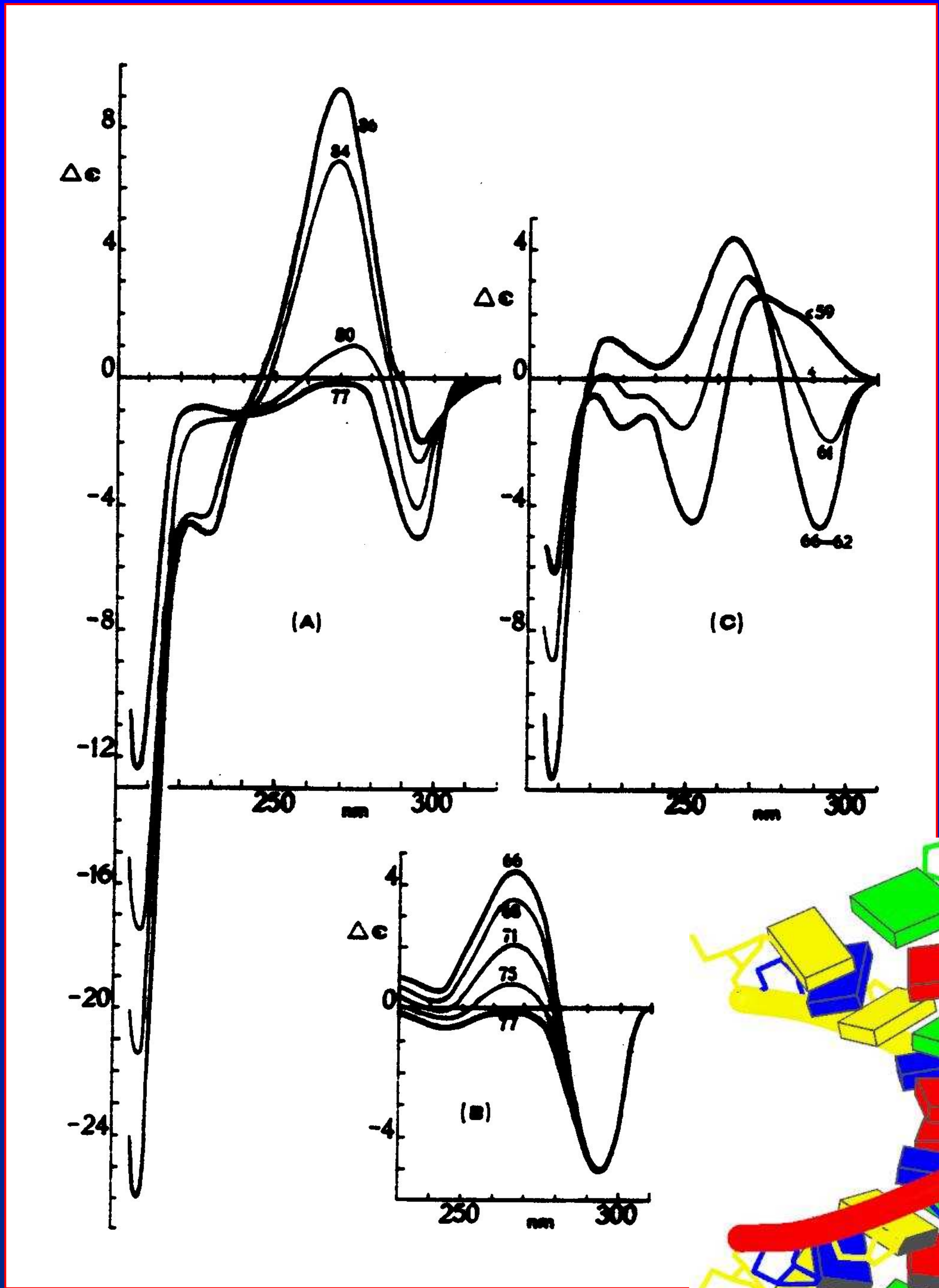
B

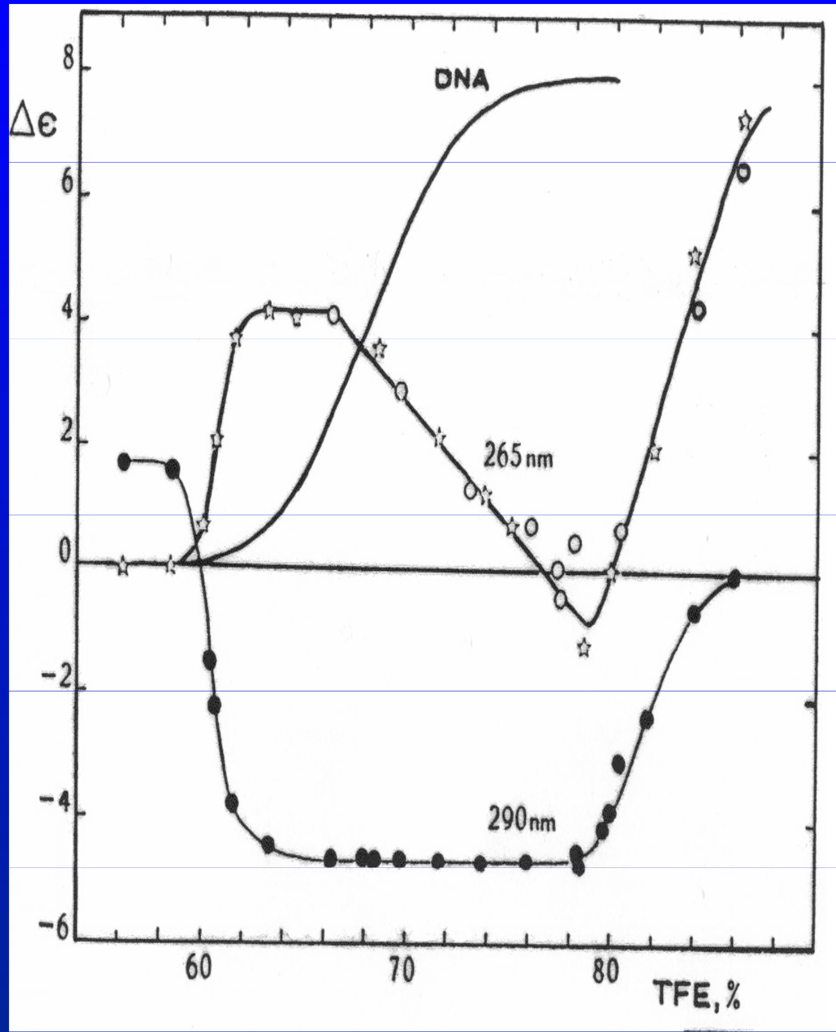


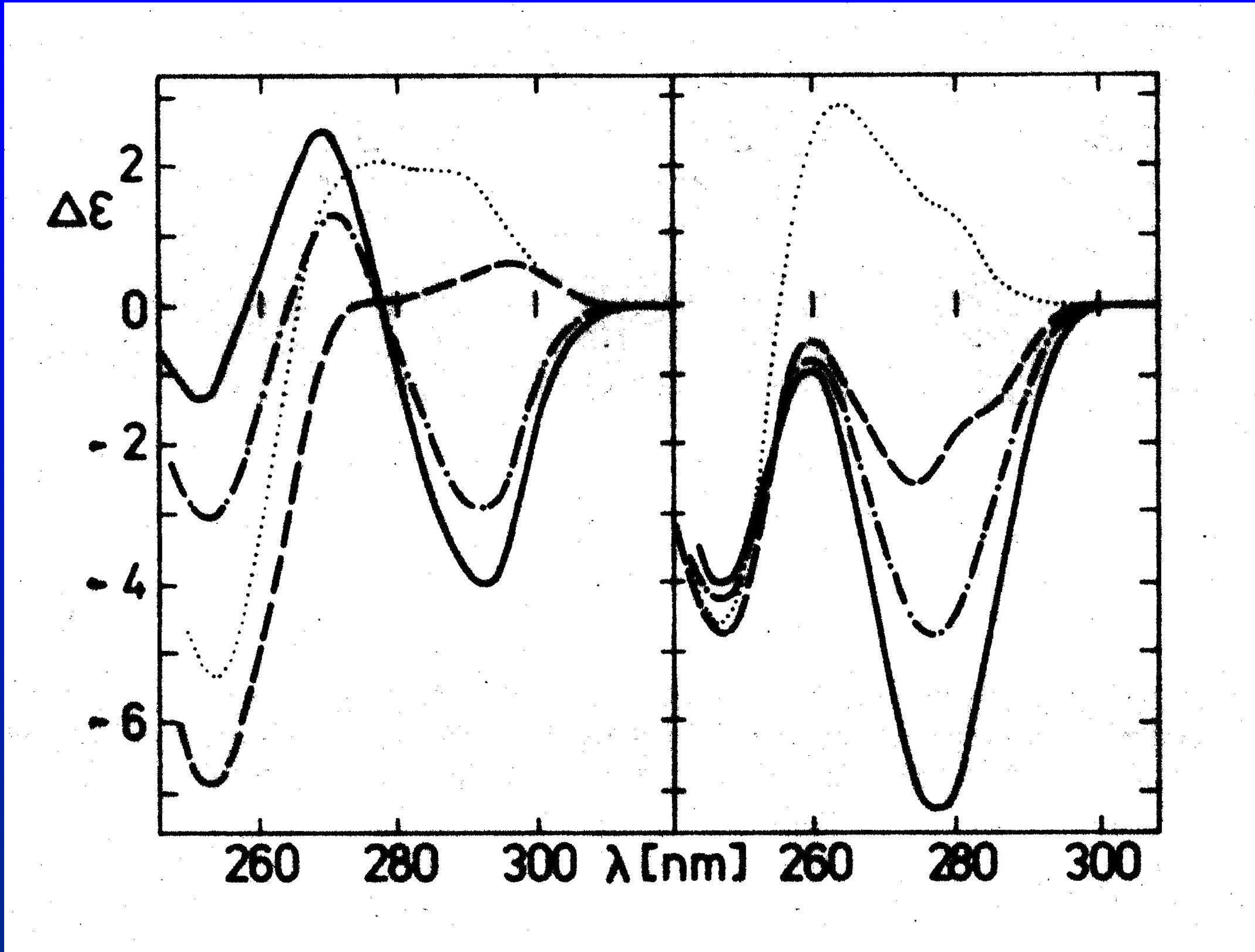

Shear
Buckle
Stretch
Propeller
Stagger
Opening
Shift
Tilt
Slide
Roll
Rise
Twist
x-displacement
inclination
y-displacement
tip
Coordinate frame

CD spectral changes accompanying B-Z transition of poly(dG-dC)

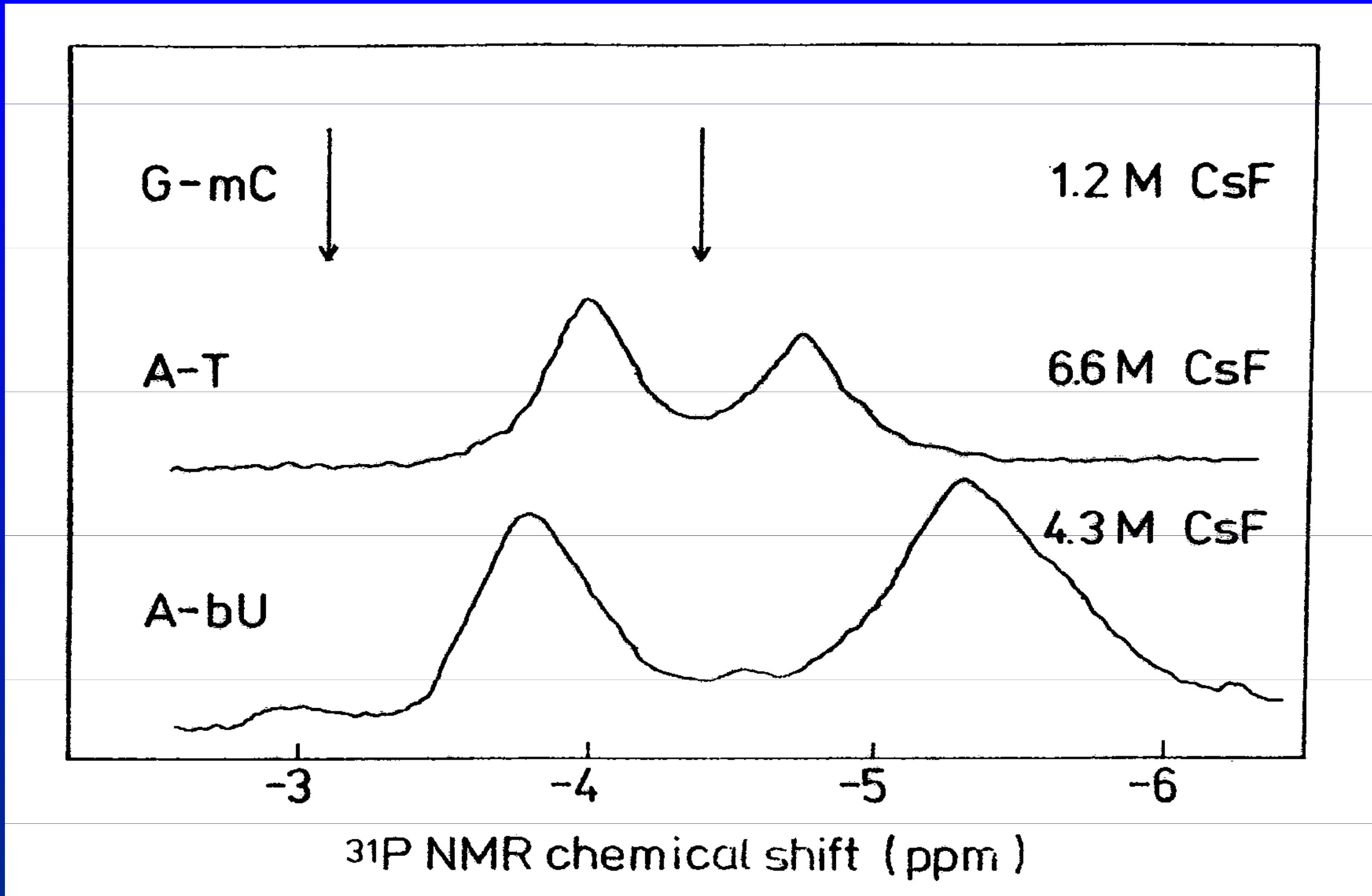


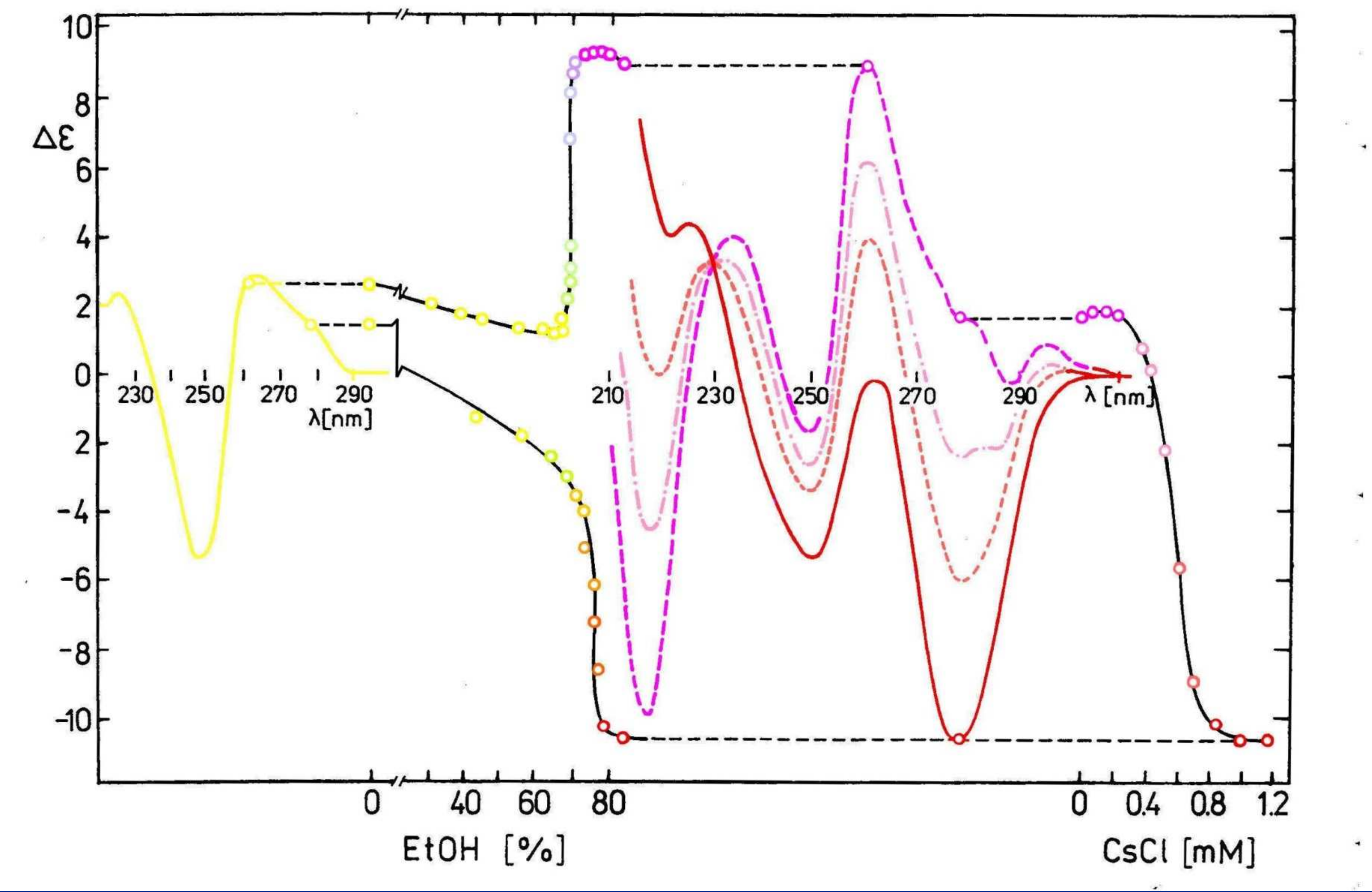

Δε
8
4
0
-4
-8
-12
-16
-20
-24
86
84
80
77
(A)
250
nm
300
c59
61
66–62
(C)
66
68
71
75
77
(B)


Δε
DNA
265 nm
290 nm
60
70
80
TFE, %

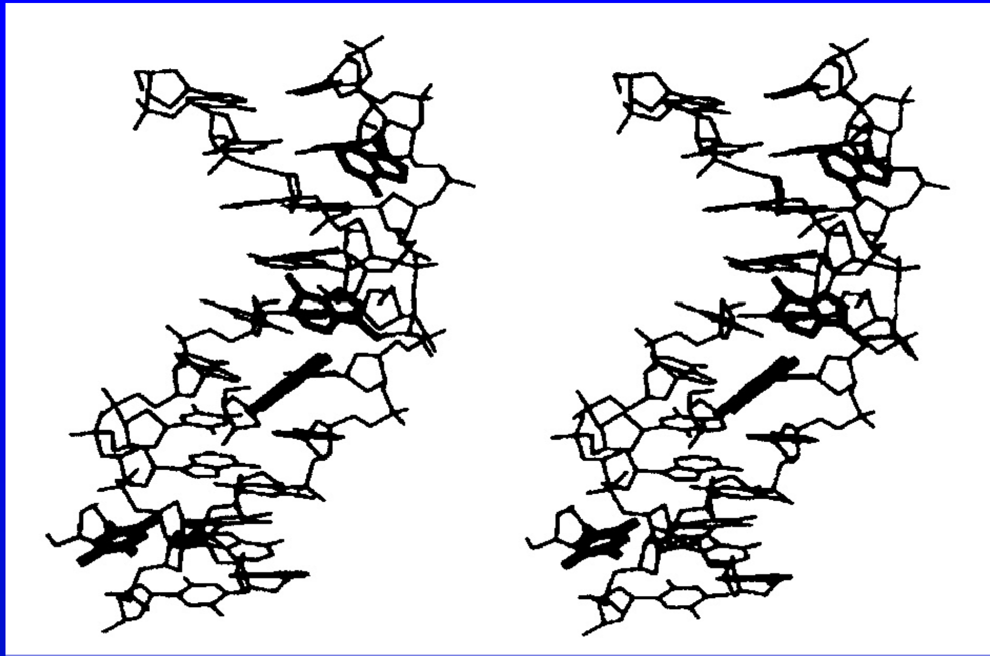


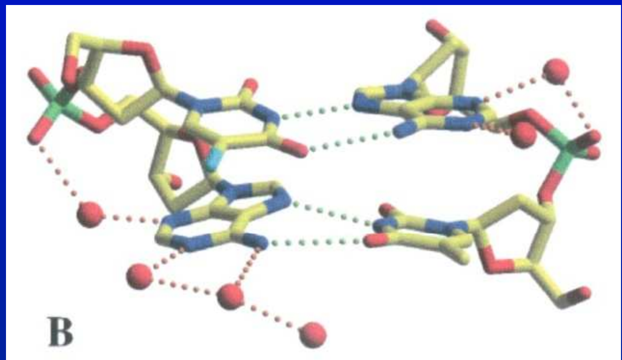
Δε
2
0
- 2
- 4
- 6
260
280
300
λ [nm]
260
280
300

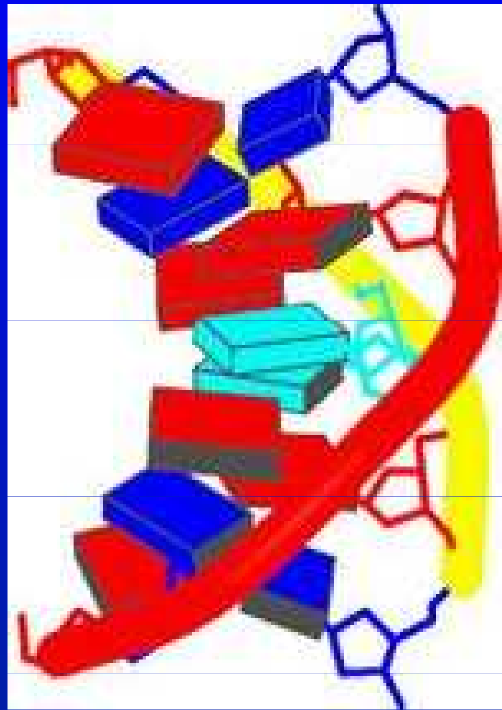

G-mC
1.2 M CsF
A-T
6.6 M CsF
4.3 M CsF
A-bU
-3
-4
-5
-6
31P NMR chemical shift (ppm)



Δε
10
8
6
4
2
0
2
-4
-6
-8
-10
230
250
270
290
λ[nm]
210
230
250
270
290
λ [nm]
0
40
60
80
EtOH [%]
0
0.4
0.8
1.2
CsCl [mM]







ALTERNATING A-T FRAGMENT WITH HOOGSTEEN BASE PAIRING

Subirana, J. *Proc.Nat.Acad.Sci.USA* , **99**, pp. 2806, 2002.
Biochemistry , **43**, pp. 4092 - 4100, 2004.

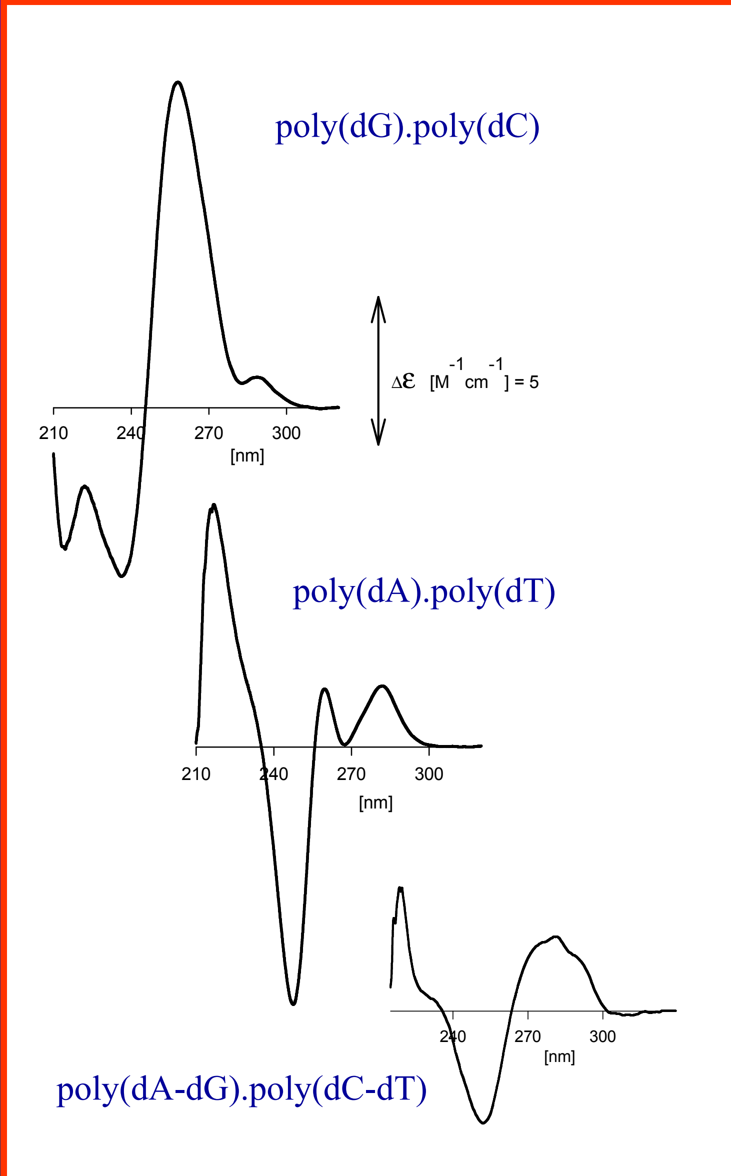
Alternating $(Pu\text{-}Py)_n$

$(Pu)_n \cdot (Py)_n$ complexes

… [G C G C G C / C G C G C G] …

… [A T A T A T / T A T A T A] …

… [A C A C A C / T G T G T G] …



[G G G G G G / C C C C C C] …

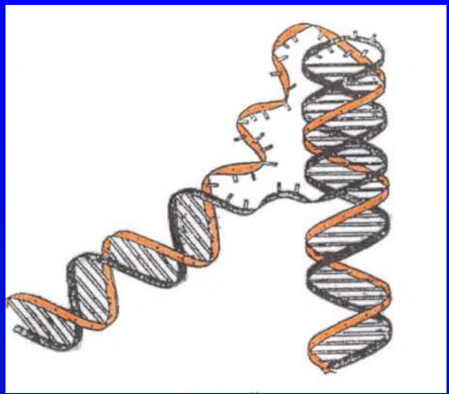
[A A A A A A / T T T T T T] …

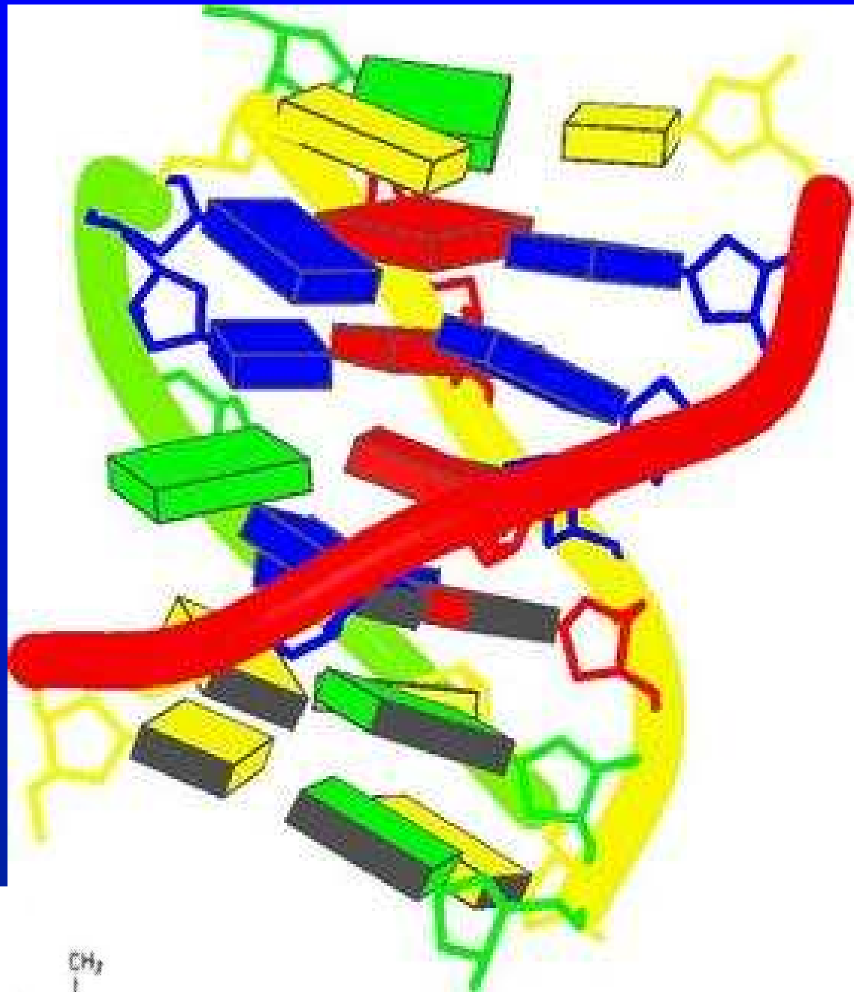
[A G A G A G / T C T C T C] …

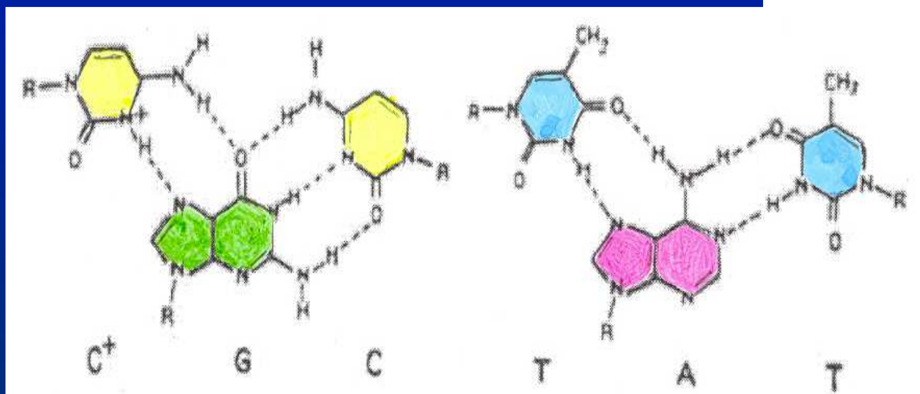
DNA Triplex

Pyrimidine. Purine. Pyrimidine

C C T A T T C
G A A T AG G
C T T G T C C



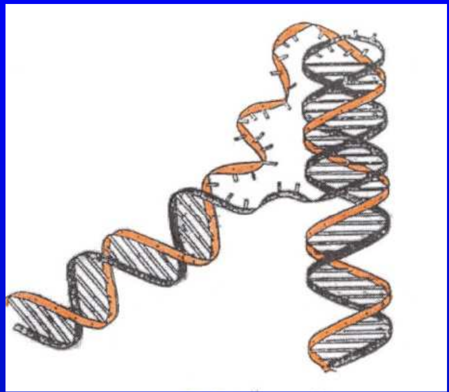


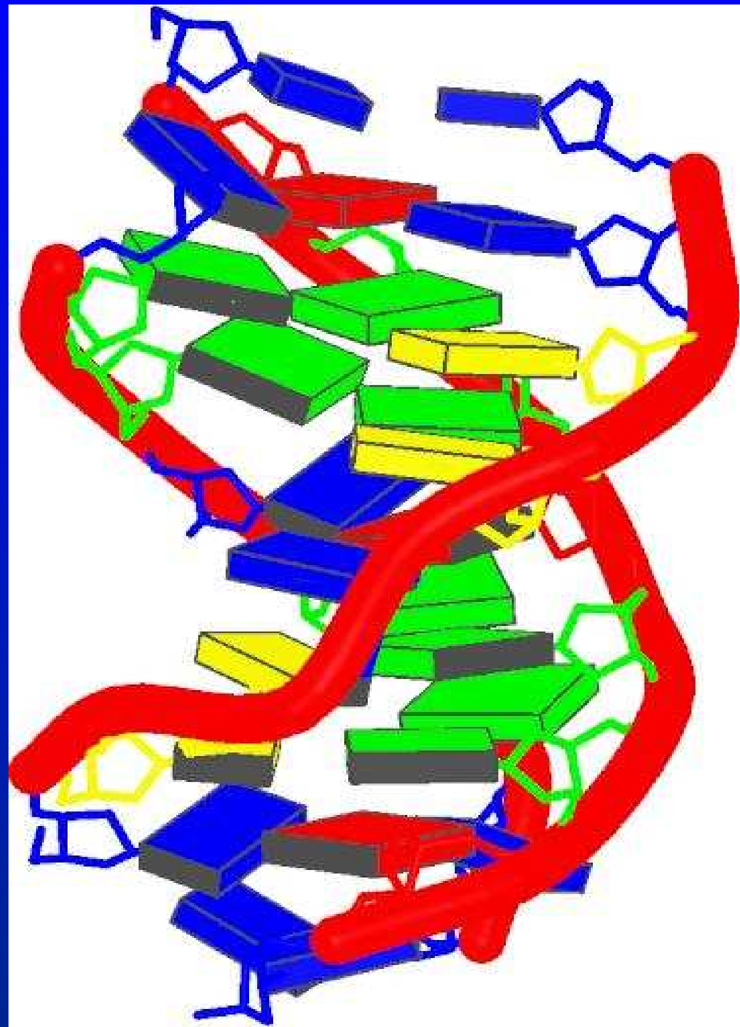


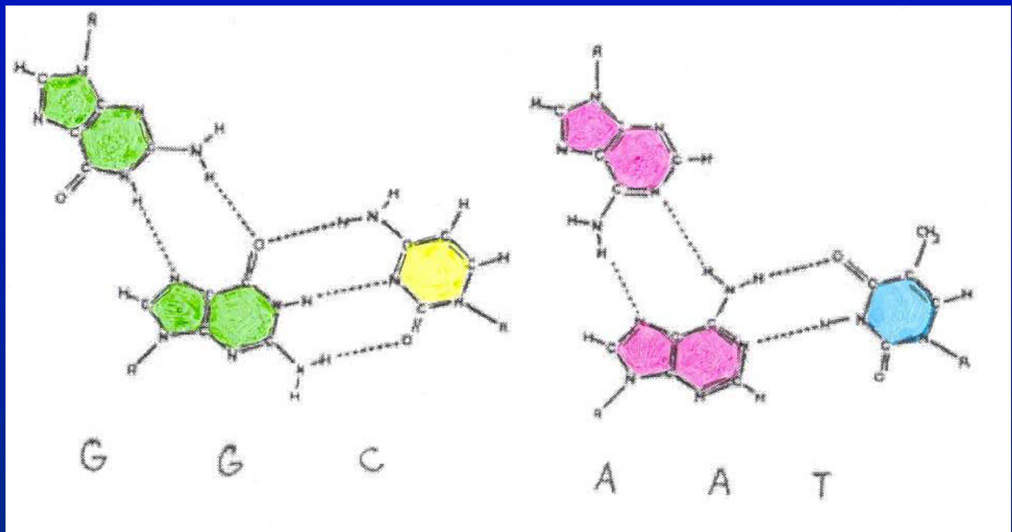
Radhakrishnan, I., Patel, D.J. (1994)

DNA TRIPLEX

T C C T C C T T T T T T A G G A G G A T T T T T T G G T G G T

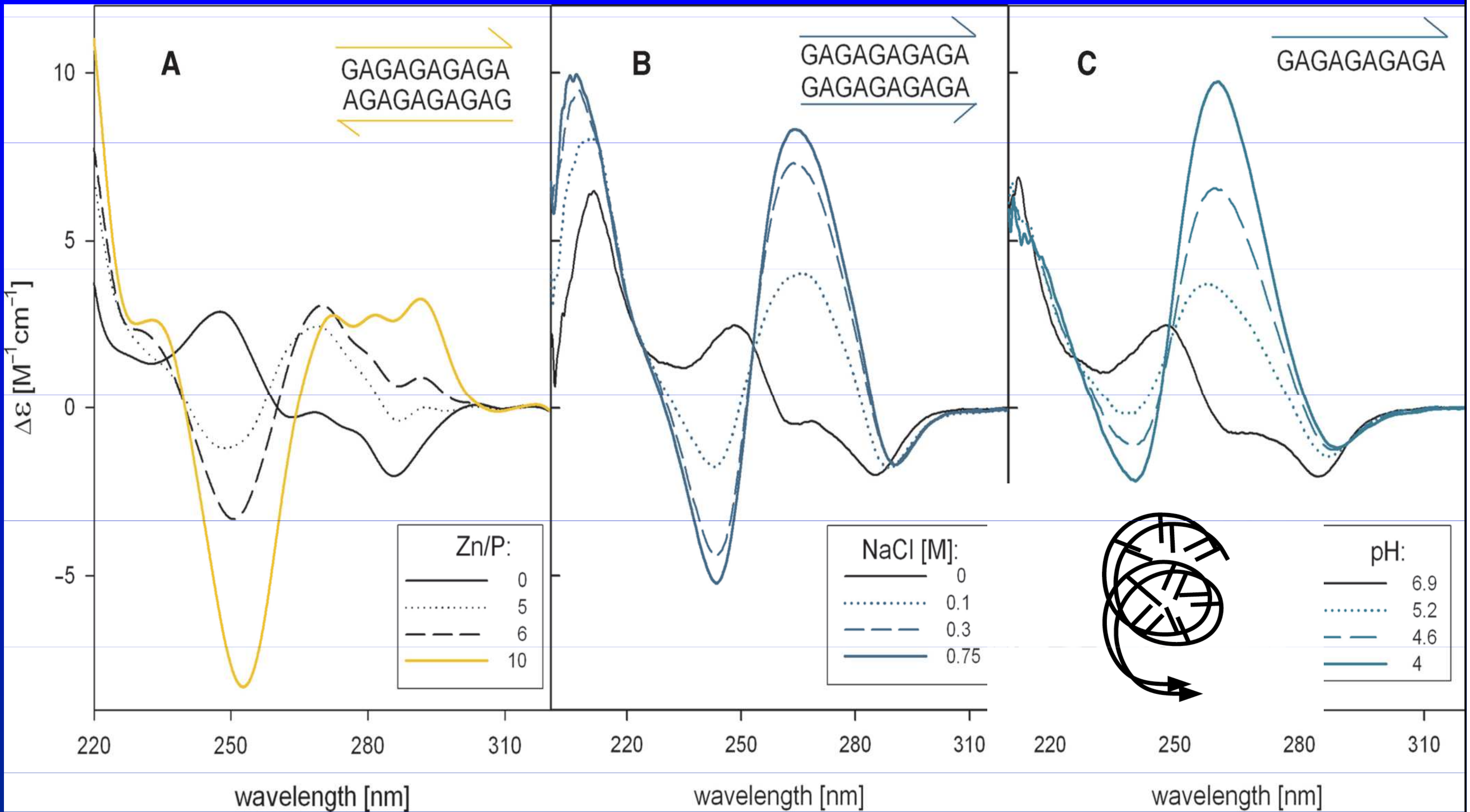






Radhakrishnan, I., Patel, D.J. (1993)

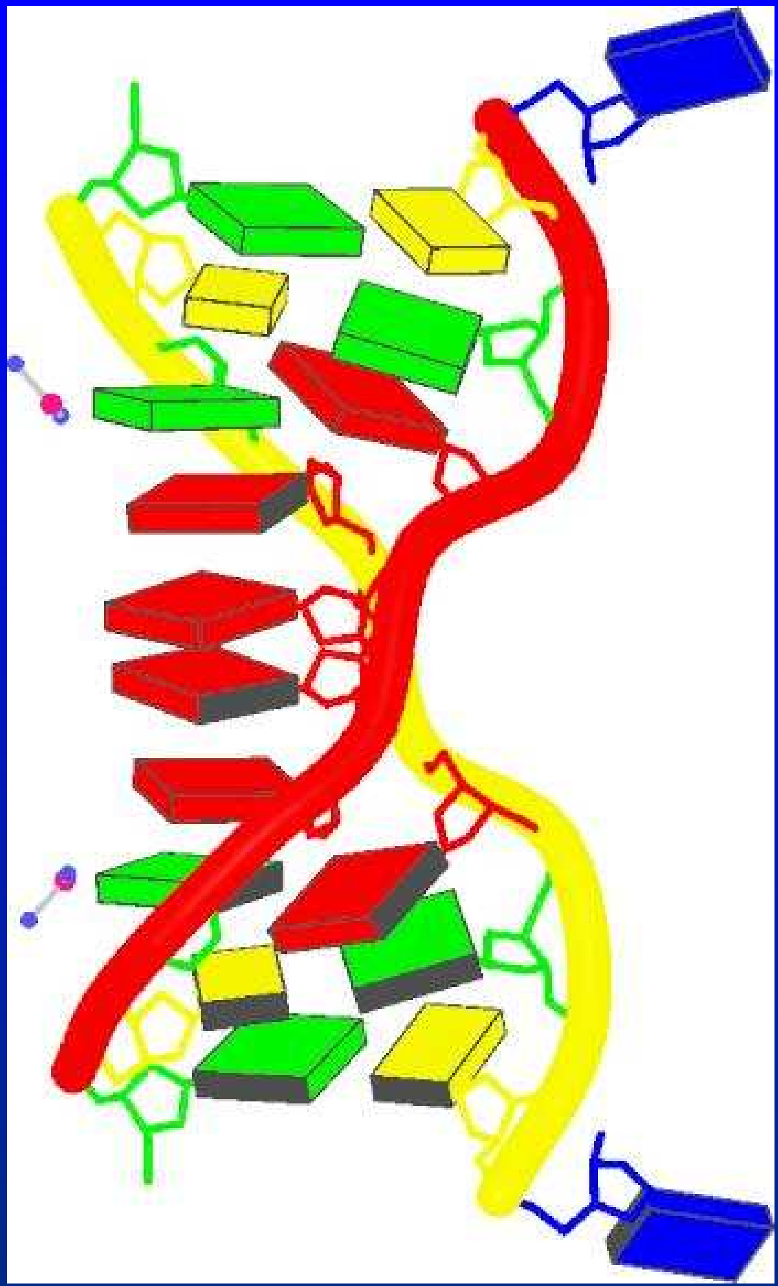
Pyrimidine. Purine. Purine



A
GAGAGAGAGA
AGAGAGAGAG
Zn/P:
0
5
6
10
B
GAGAGAGAGA
GAGAGAGAGA
NaCl [M]:
0
0.1
0.3
0.75
C
GAGAGAGAGA
pH:
6.9
5.2
4.6
4
Δε [M⁻¹cm⁻¹]
10
5
0
-5
220
250
280
310
wavelength [nm]
wavelength [nm]
wavelength [nm]

A ZIPPER-LIKE DNA DUPLEX

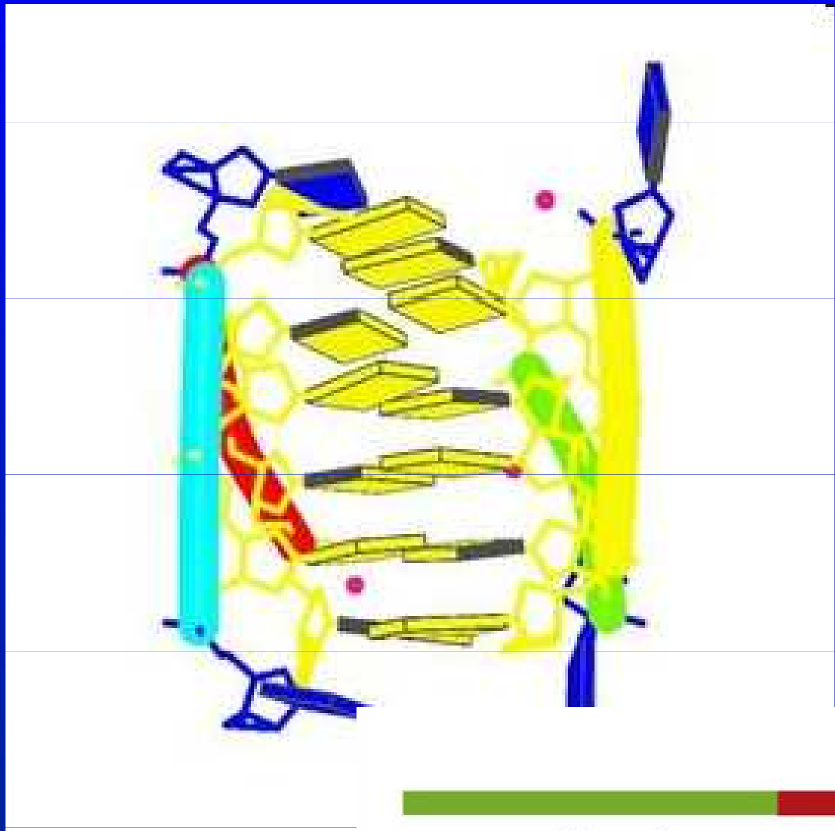
d(GCGAAAGCT)

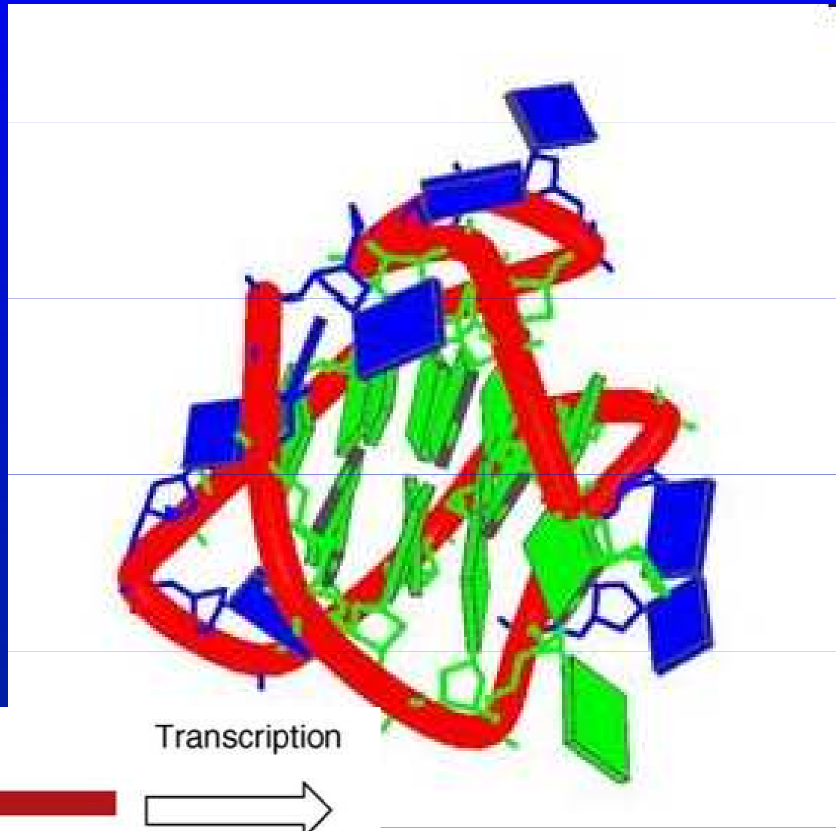


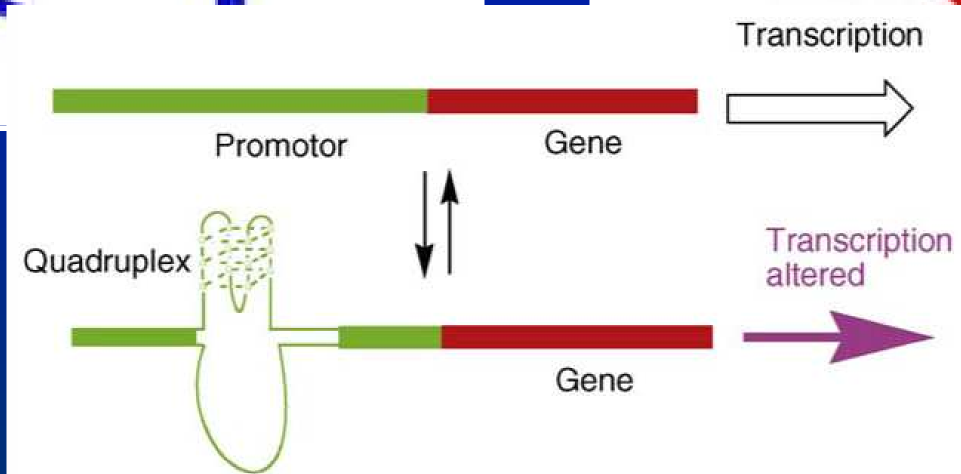
Shepard, W. et al.,
Structure **6**, pp. 849 - 861, 1998.

Quadruplexes

frequently occur in promoters of genes and were shown to control their expression.

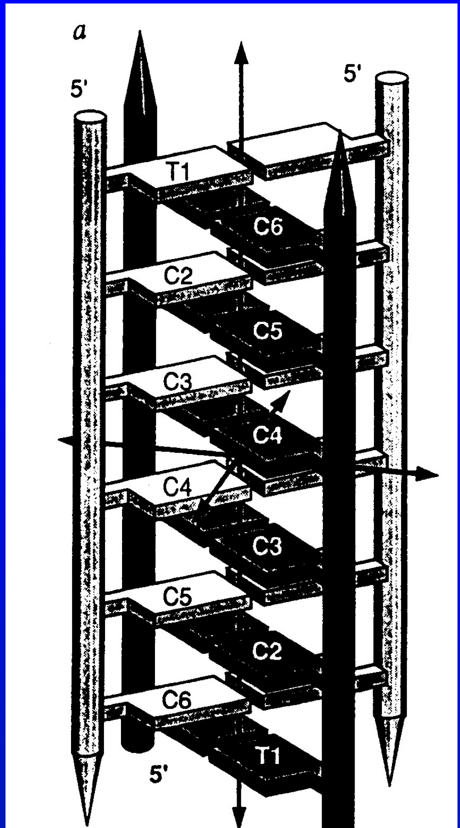




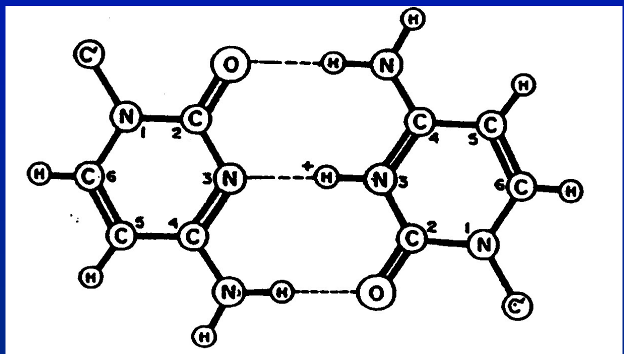


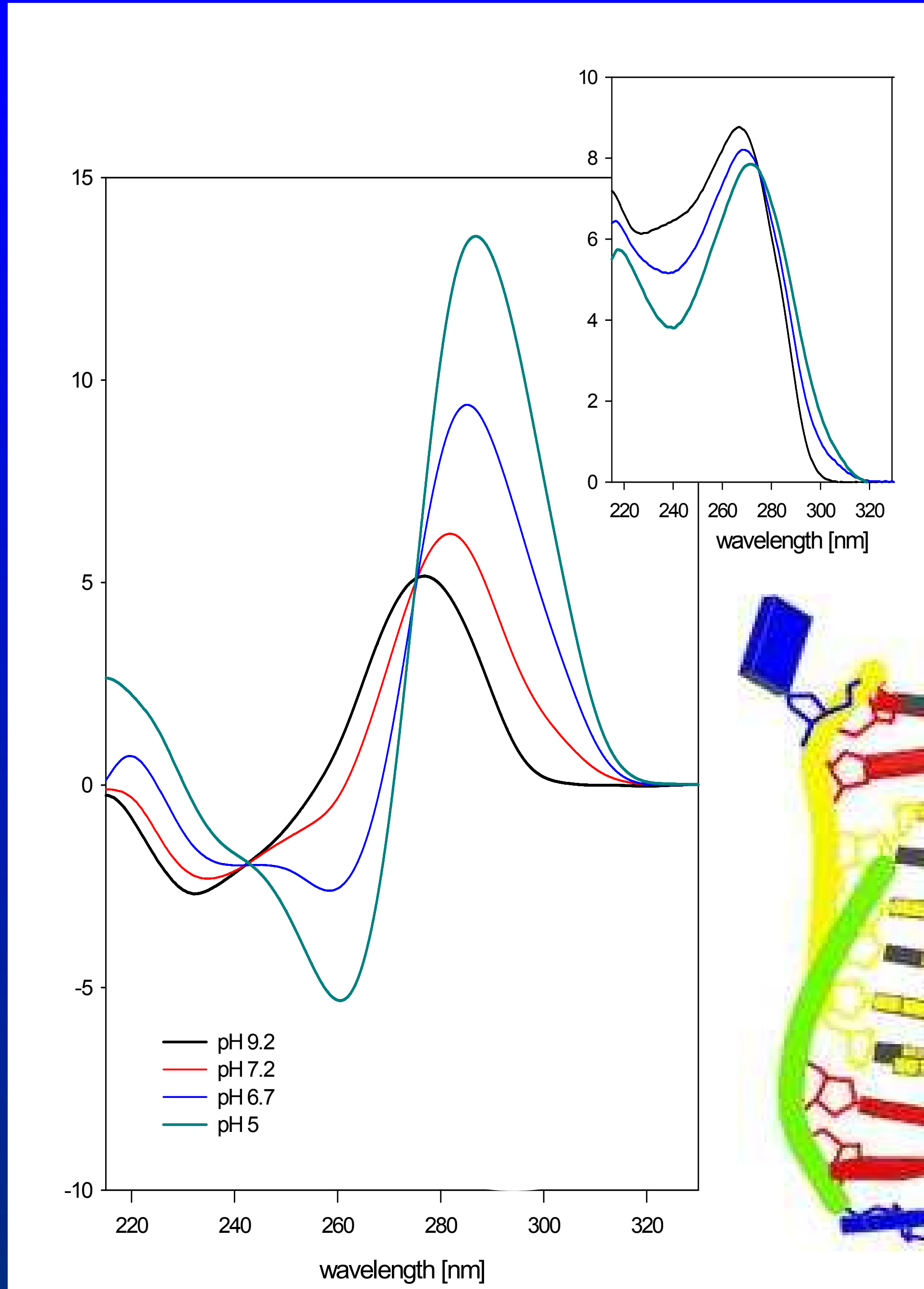
Wang, Y., Patel, D.J. (1994)

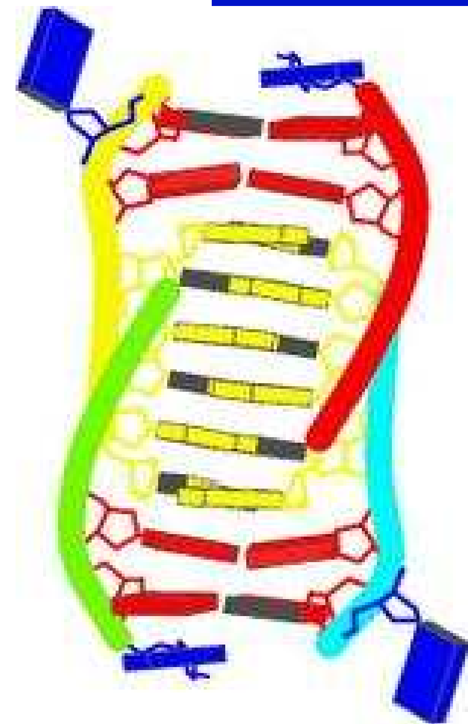
i - tetraplex



Leroy, J.L., Gueron, M.,1995

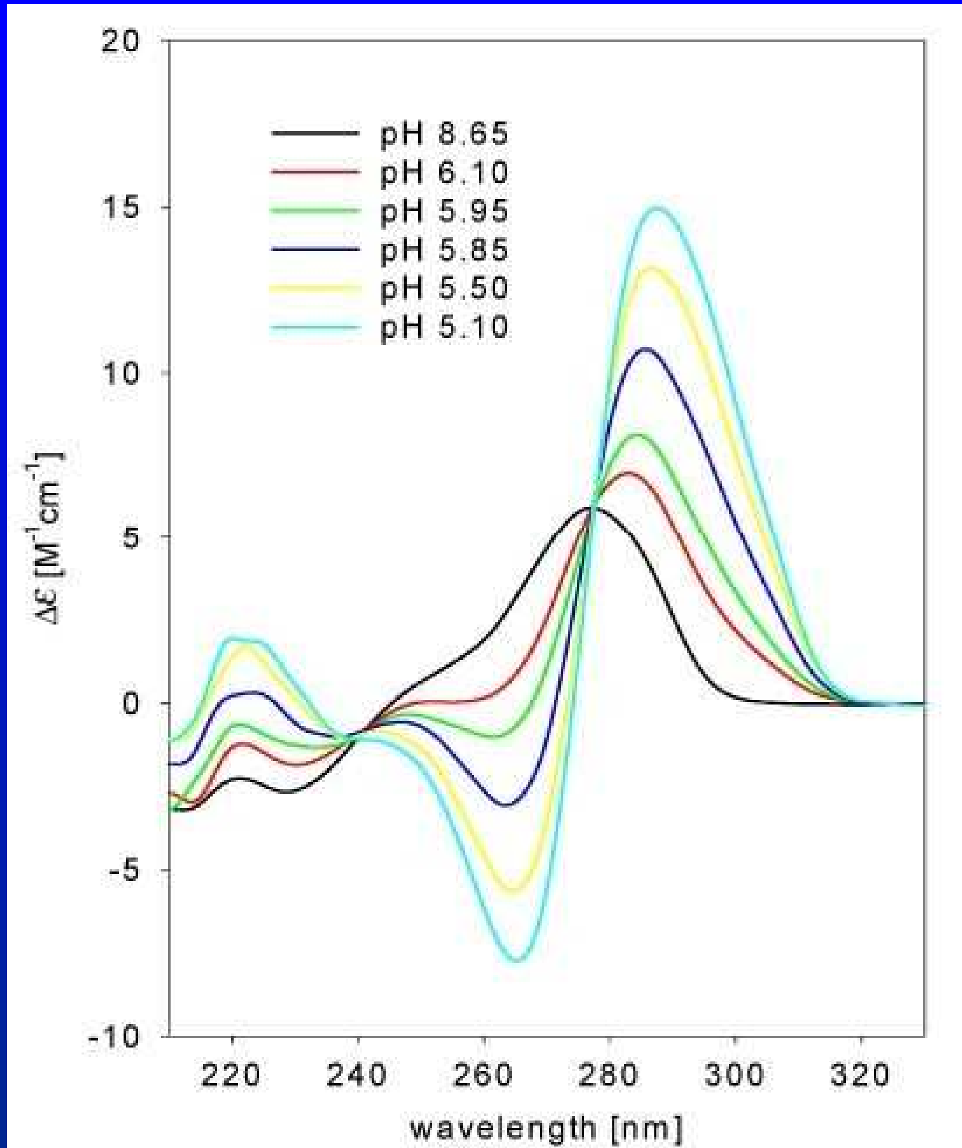




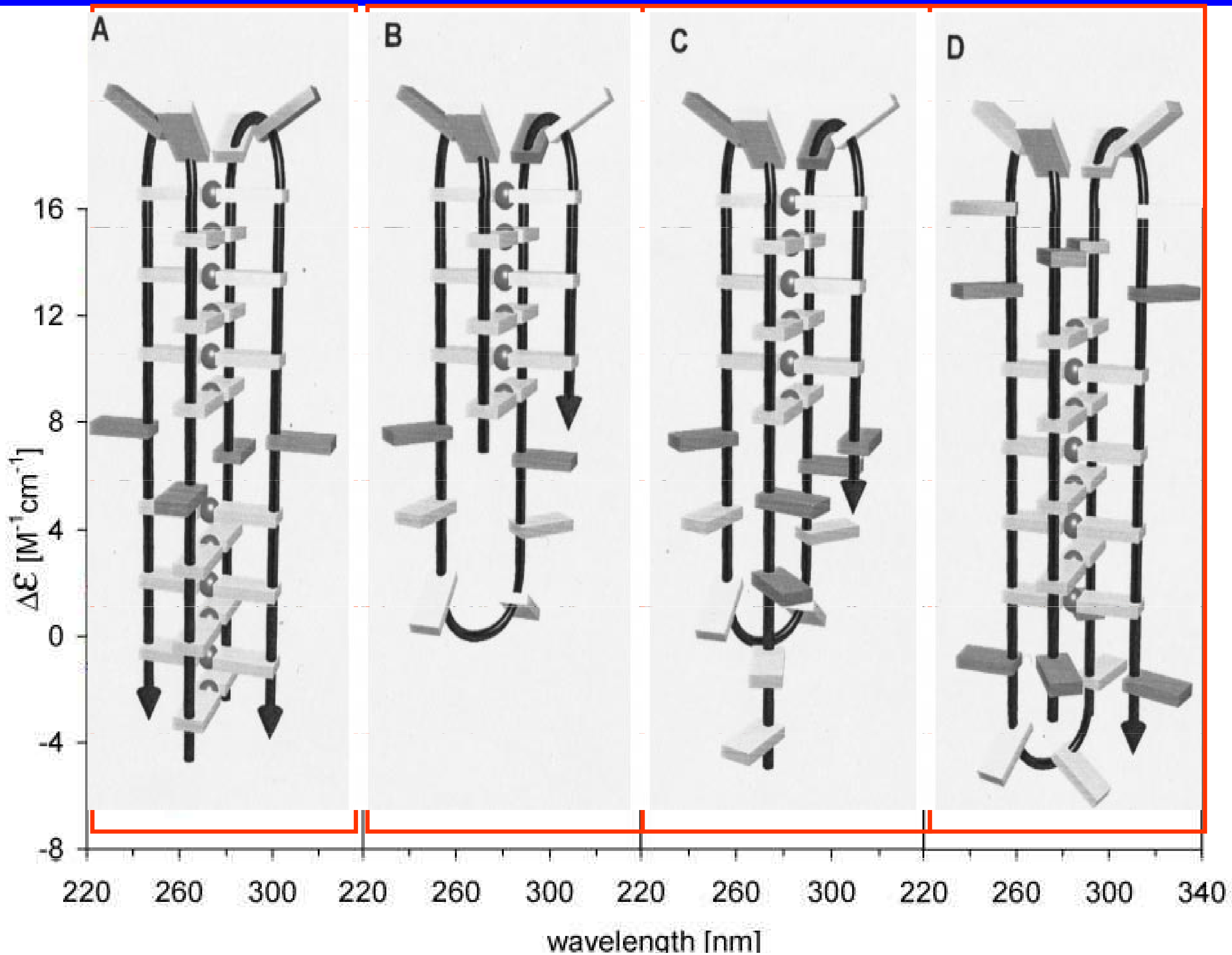


Two parallel-bonded duplexes are intercalated in the antiparallel fashion

Intercalated tetraplex of human telomeric DNA



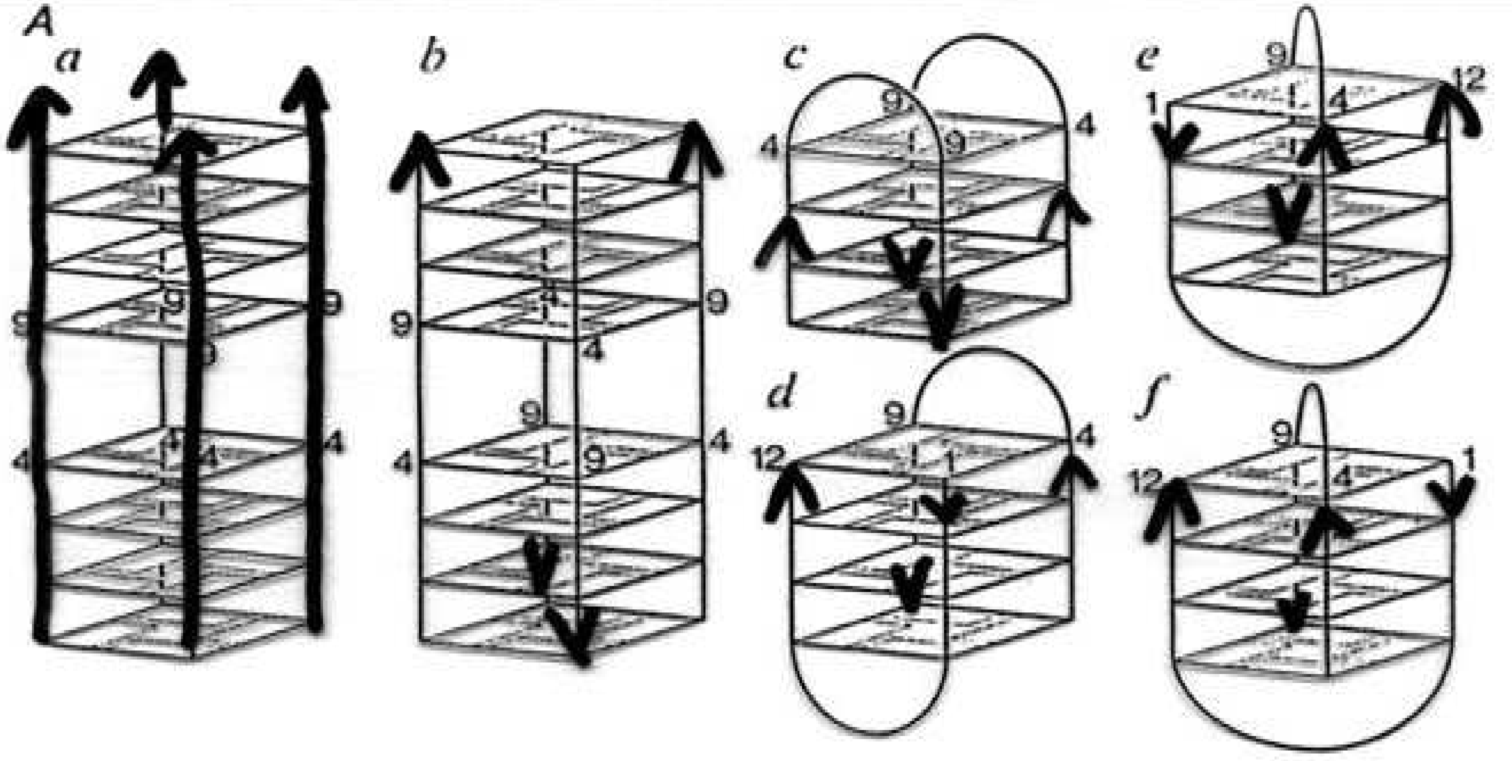
Berger, I., Kang, C., Fredian, A., Ratliff, R., Moyzis, R., Rich, A.
Nat.Struct.Biol., **2**, pp. 416 - 25, 1995



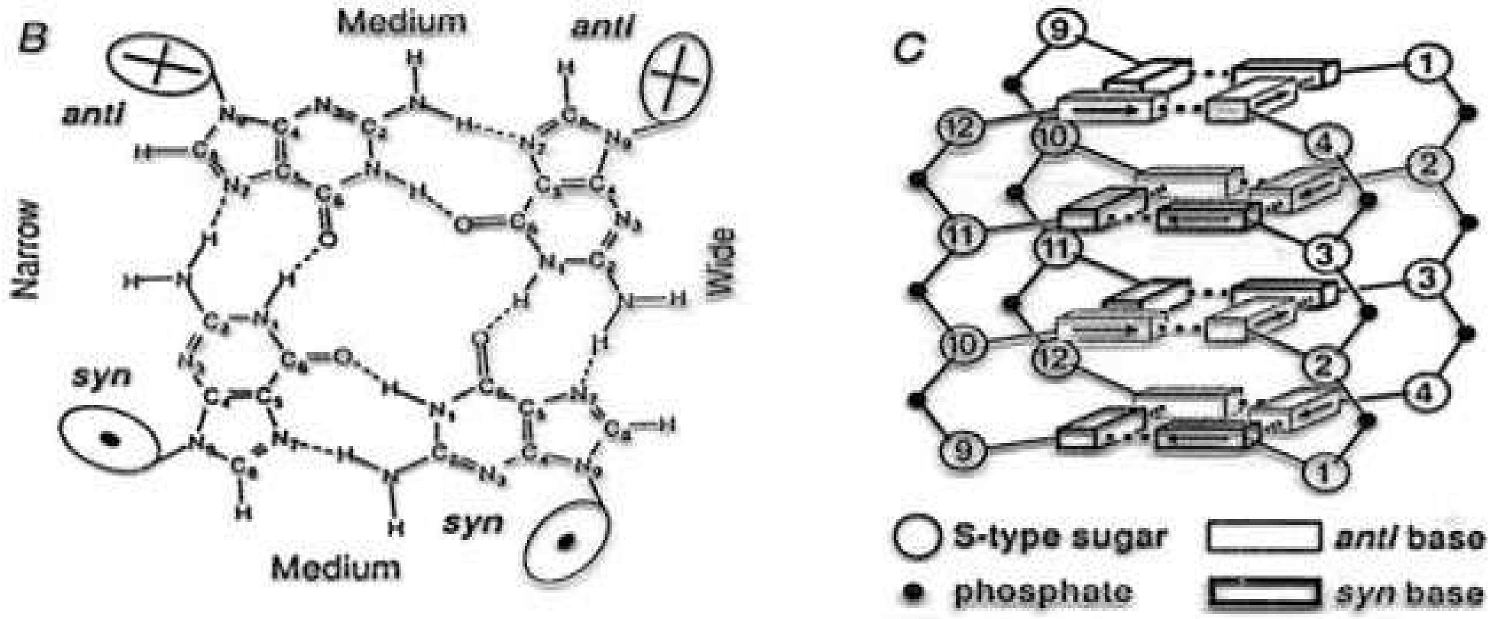
Fragment in c-myc promoter

TCCCCA CCTT CCCCA CCCTCCCCACCCTCCCC C A

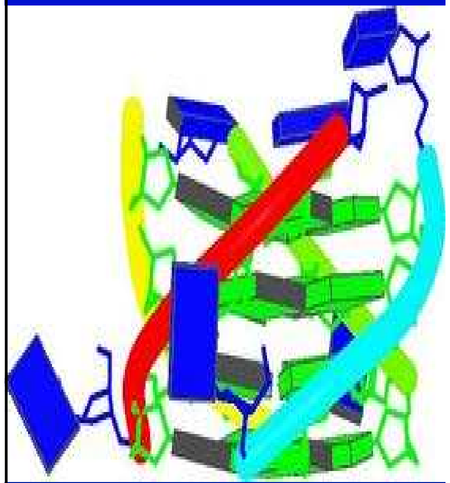
Q
DNA

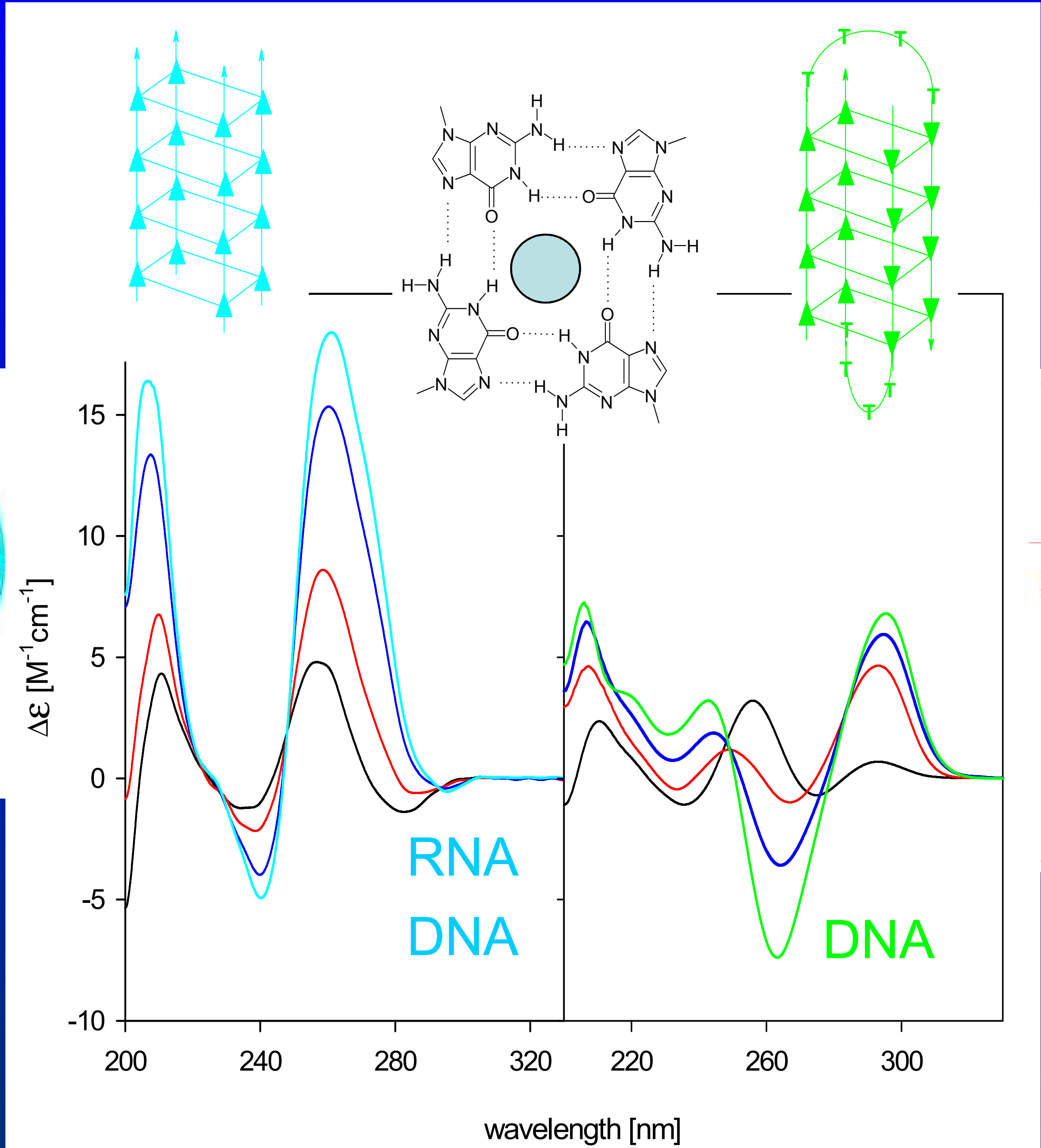


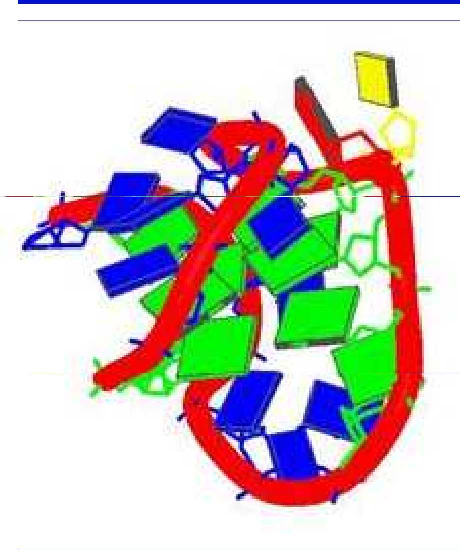
G - quadruplex



CD spectra reflecting formation of a parallel and antiparallel guanine quadruplex

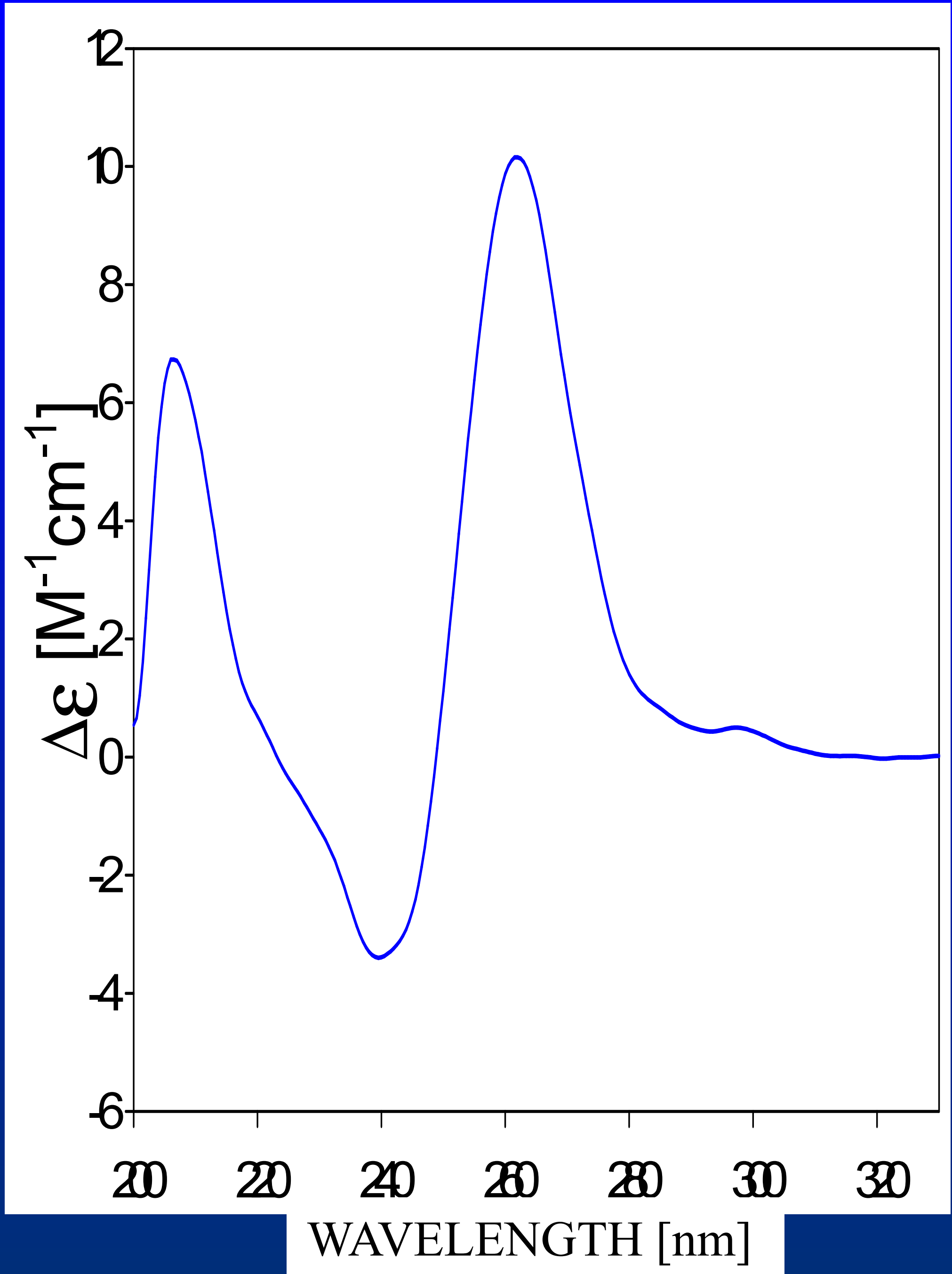


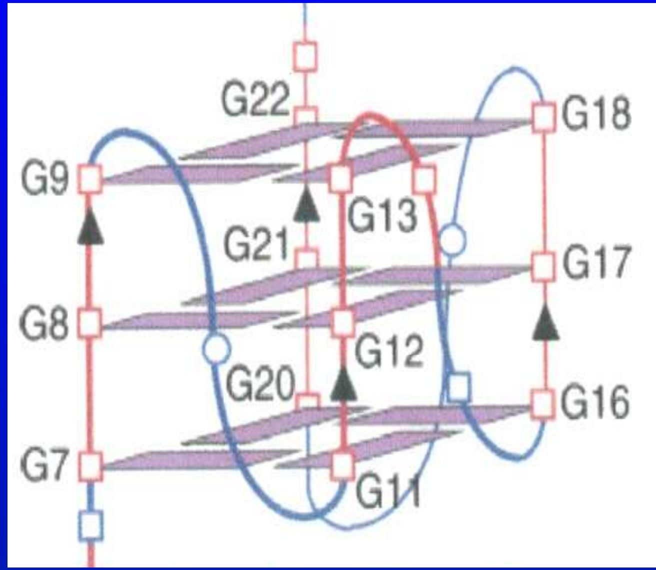




Fragment Pu-27 of c-myc promoter:

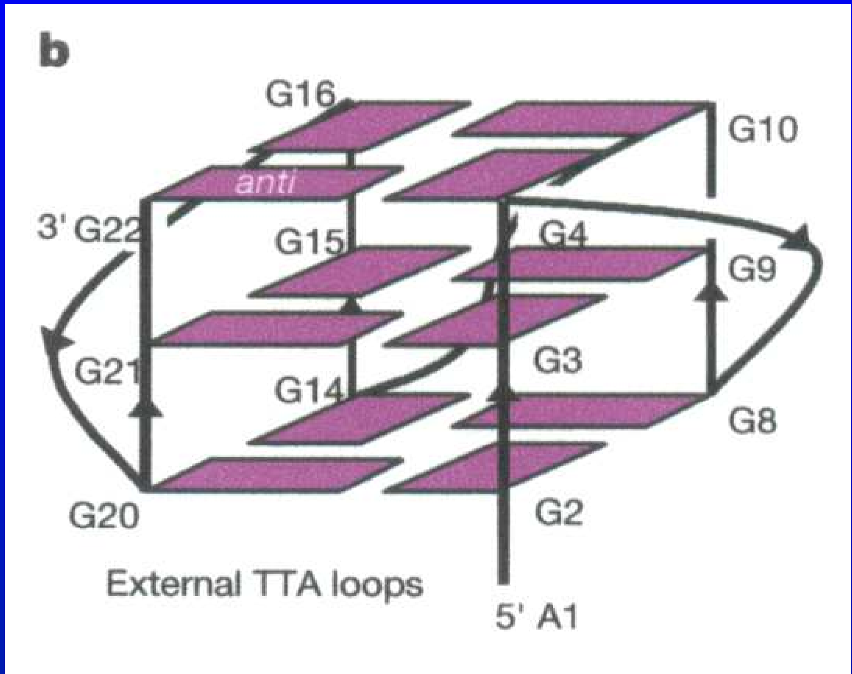
TGGGGAGGGTGGGGAGGGTGGGGAAGG

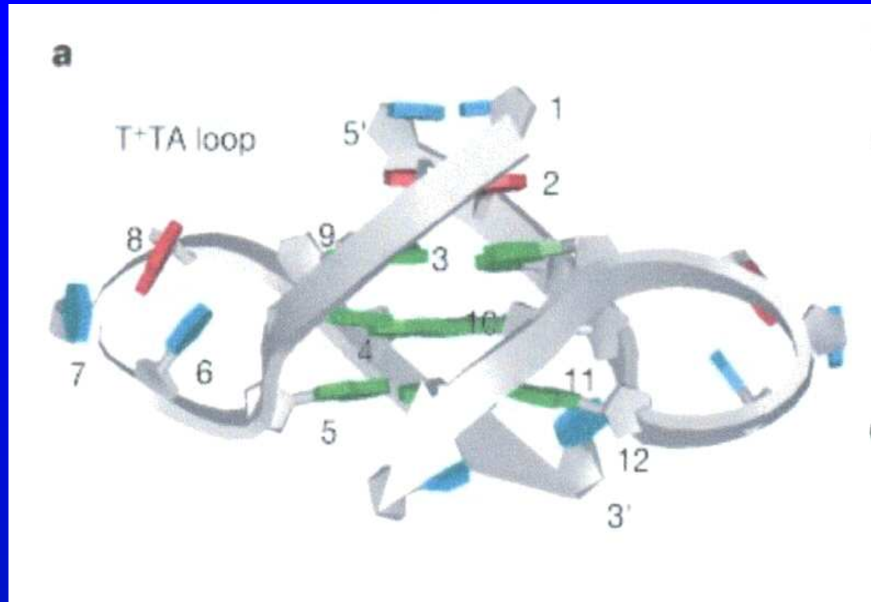


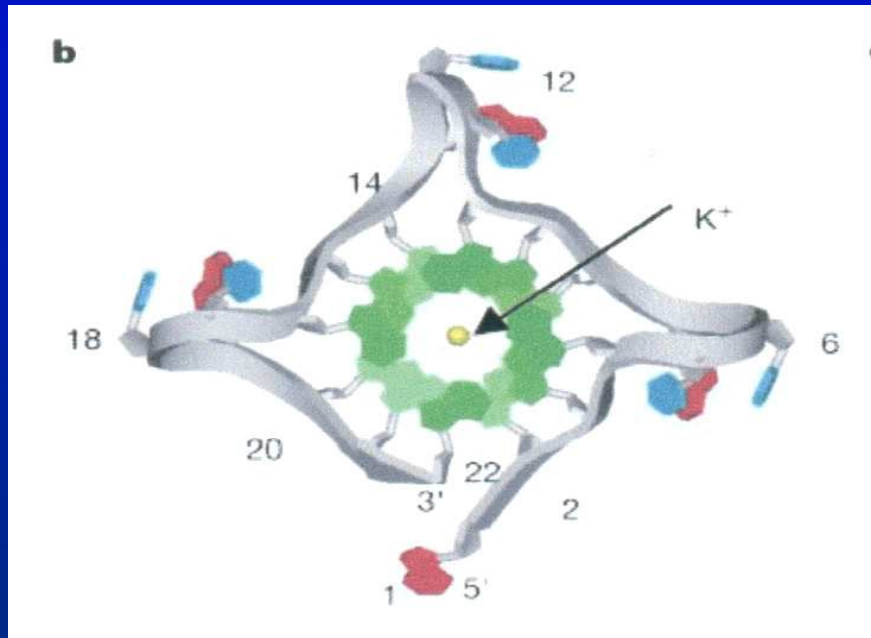


Pan, A.T. et al.:
J.Am.Chem.Soc. **126**(2004)8710

d(TAGGGTTAGGGT) 12



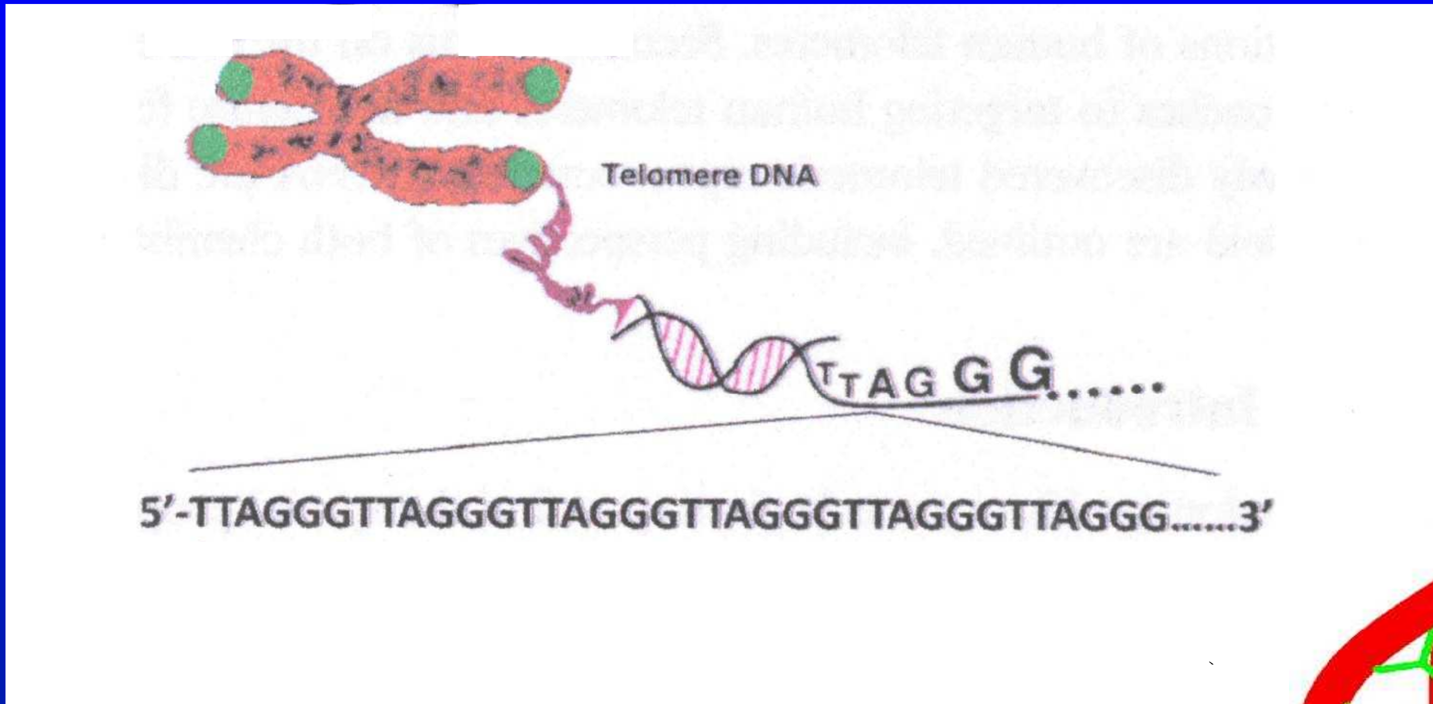


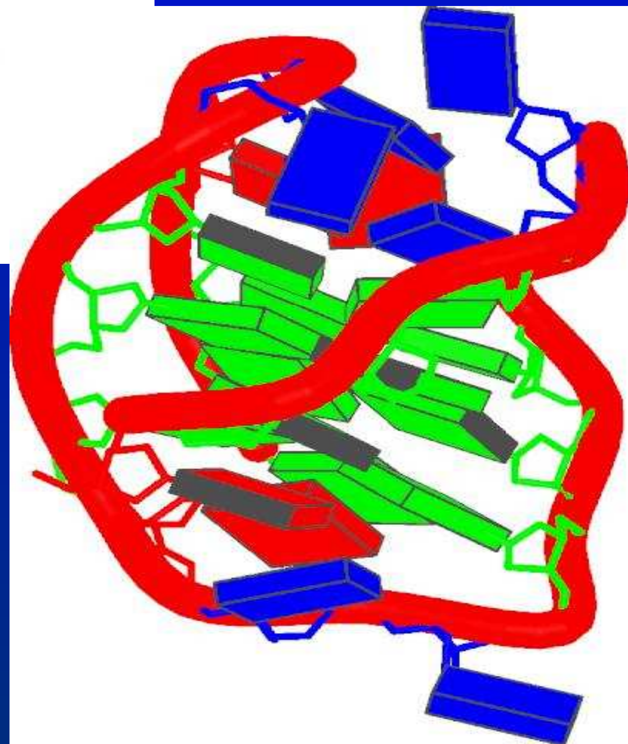


Parkinson, G.N., Lee, M.P.H, Neidle, S. *Nature* **417** (2002) 876-880.

d[AGGG(TTAGGG)3] 22

Human telomeric DNA forms quadruplex



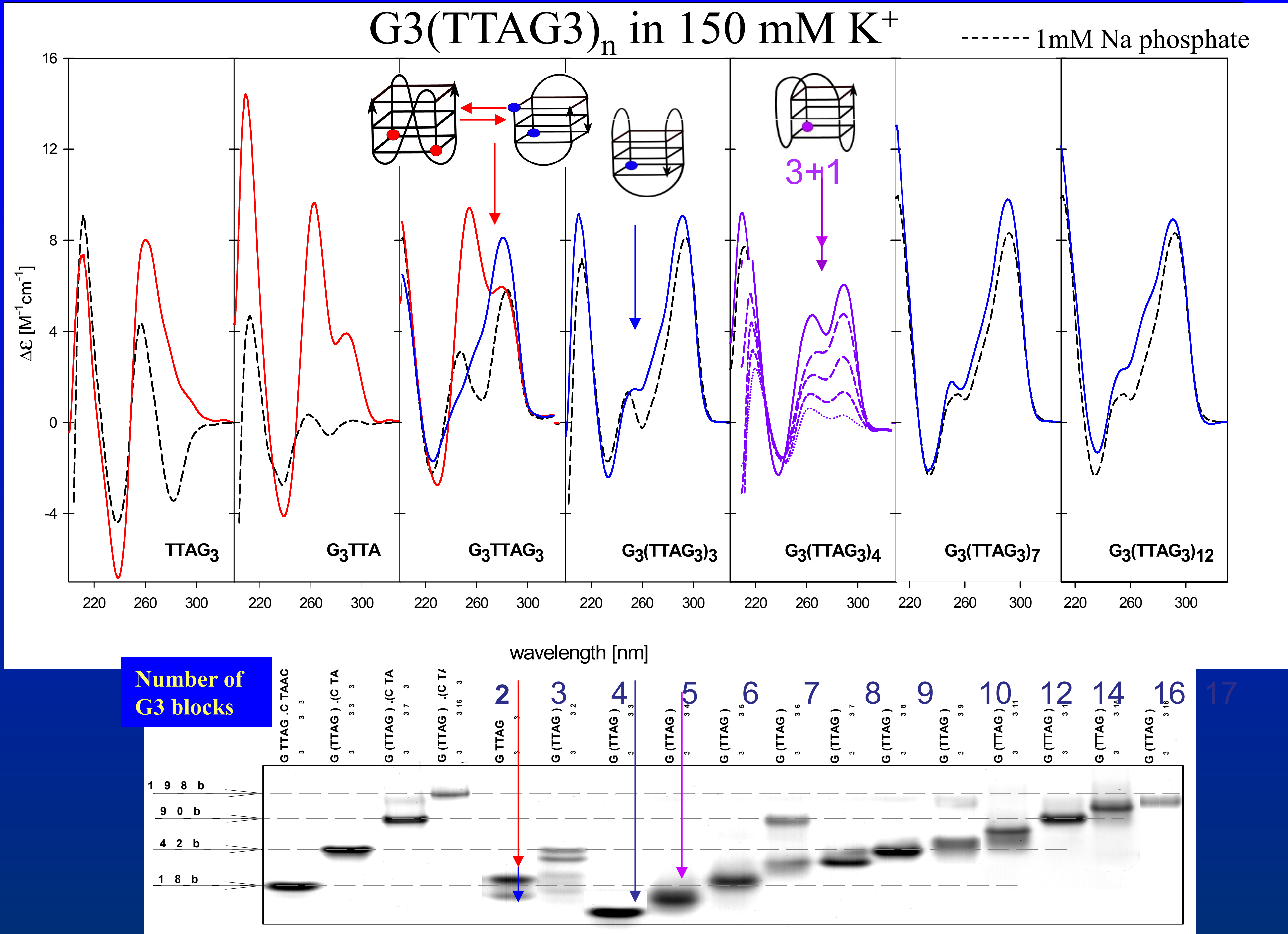


Telomeric DNA is associated with aging

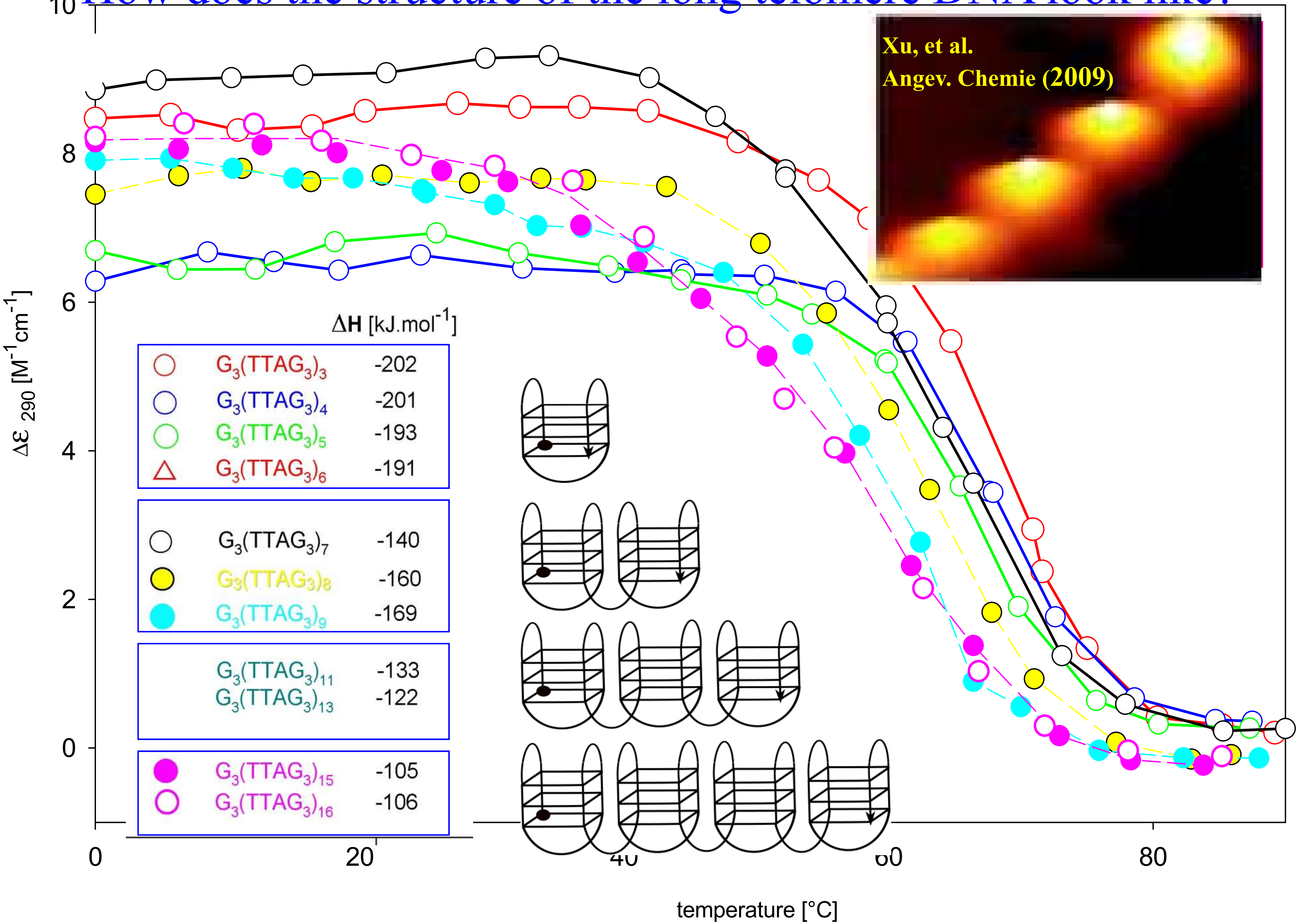
The telomere quadruplex became a target for developing anticancer drugs

Guanine quadruplex topology of human telomere DNA is governed by the number of (TTAGGG) repeats.

Nucleic Acids Res. **33** (2005) 5851-5860.

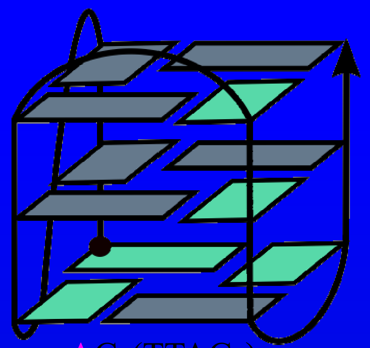


How does the structure of the long telomere DNA look like?



What is the structure of the bead?

3 + 1



A$G_3(TTAG_3)_3$

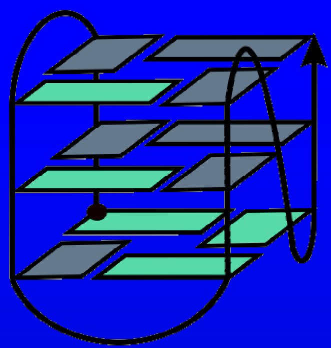
TA$G_3(TTAG_3)_3$

AAA$G_3(TTAG_3)_3$AA

Luu, et al.: J.Am.Chem.Soc., 128 (2006) 9963-9970.

Ambrus, et al.: Nucleic Acids Res. 34 (2006) 2723–2735.

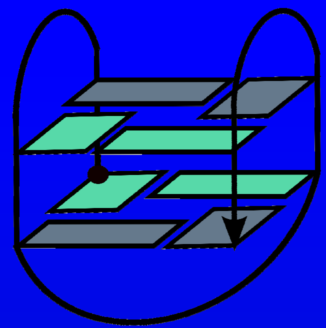
3 + 1



TA$G_3(TTAG_3)_3$TT

Phan, at al.: Nucleic Acids Res. 34 (2006) 5715-5719.

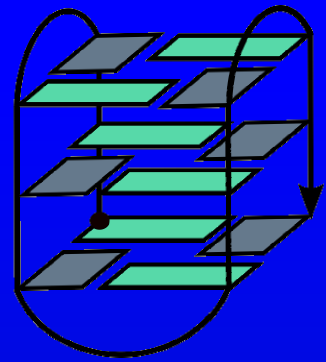
BASKET
two tetrads



$G_3(TTAG_3)_3$T

Lim, et al.: J.Am.Chem.Soc. 131 (2009) 4301–4309.

CHAIR



A$G_3(TTAG_3)_3$

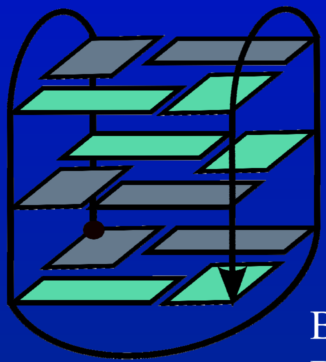
He et al.:Nucleic Acids Res. 32 (2004) 5359-5367.

Matsugami, et al.:. Nucleic acids symp. series, 50 (2006) 45-46.

Xu et al.: Bioorg.& Medicinal Chem. 14 (2006)5584 – 5591.

K^+

0.2-5 mM strand concentration in NMR
3-50 µM strand concentration in CD



$G_3(TTAG_3)_3$

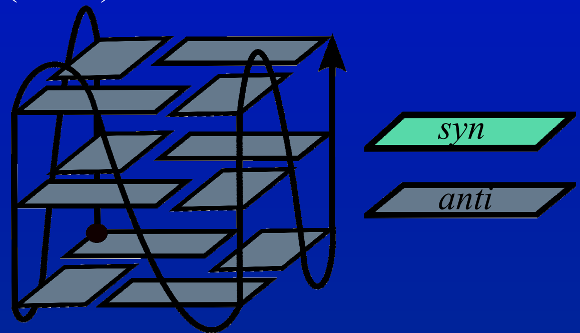
A$G_3(TTAG_3)_3$

TTA$G_3(TTAG_3)_3$

BASKET

Balagurumoorthy, Brahmachari: J. Biol. Chem. 269 (1994) 21858-21869.

Redon et al.: Nucleic Acids Res. 31 (2003) 1605-1613.



A$G_3(TTAG_3$

Parkinson, Lee, Neidle: Nature 417 (2002) 876-880.

PARALLEL

What may be the reason that different quadruplex structures were observed by various methods?

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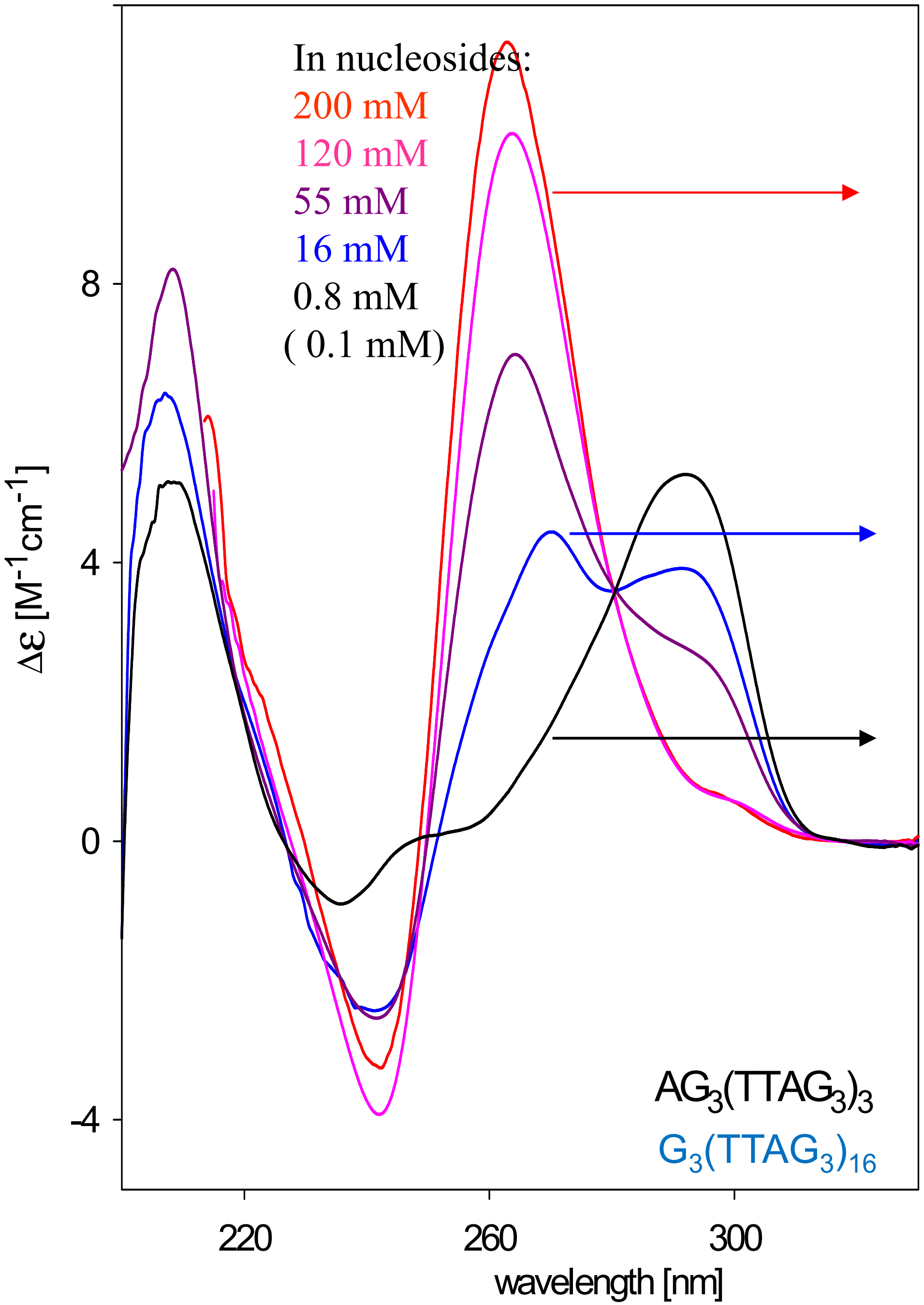

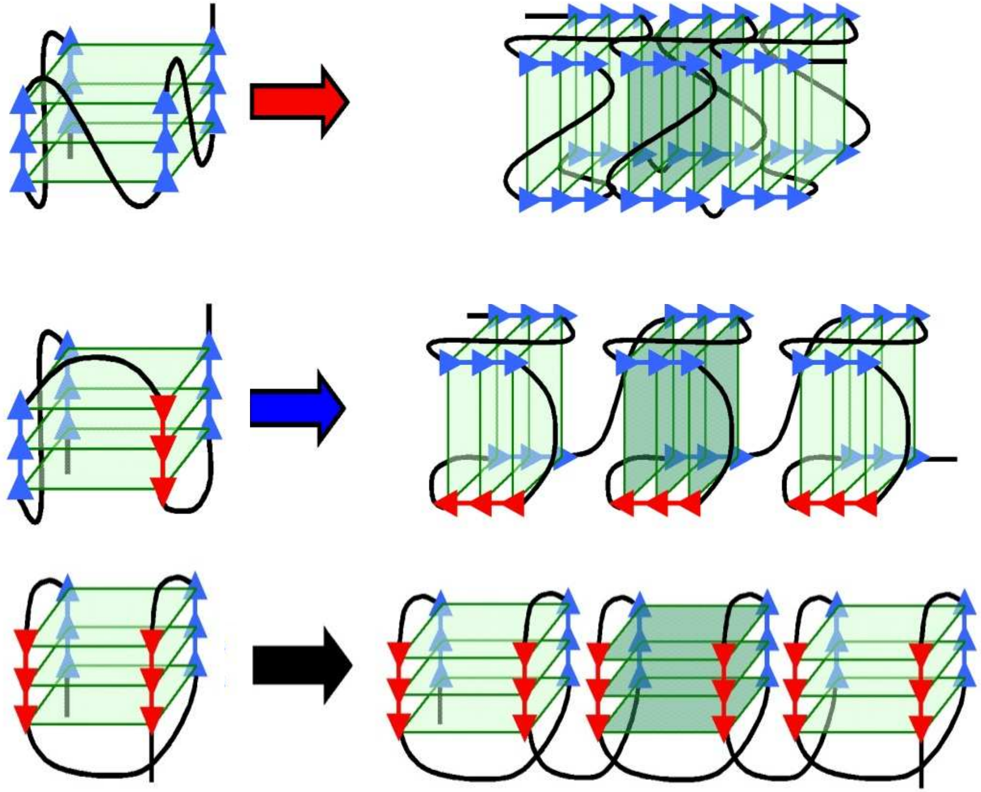

The arrangement of the human telomere quadruplex is polymorphic and depends on DNA concentration.
The particular structures may perform distinct functions.