Structure and Properties of Nucleic Acid Components
Human DNA: 3 Billion Base Pairs

NET RESULT: EACH DNA MOLECULE HAS BEEN PACKAGED INTO A MITOTIC CHROMOSOME THAT IS 50,000x SHORTER THAN ITS EXTENDED LENGTH
Double Helical B DNA

Bdl001.pdb

ACGT bases.cwg
THE FOUR LETTER CODE: A, C, G, T

COMPLEMENTARY WATSON CRICK BASE PAIRING BETWEEN TWO ANTIPARALLEL STRANDS

A base recognizes T, and G recognizes C

B DNA Structure
DNA Replication: 5' to 3', template directed via Watson Crick Base Pairing
Replication of DNA

DNA Polymerase

PRIMER

TEMPLATE
DNA to RNA to PROTEIN

TRANSCRIPTION

DNA

mRNA

5'ppp

codon

anti-codon

5'

A - U

U - A

U - A

G - C

U - A

A - U

5'

tRNA

RNA to PROTEIN

3'

5'

Ribosome

TRANSLATION

aa-tRNA

5'

3'
DNA to RNA: Transcription by RNA polymerase

POLYMERIZATION

RNA Polymerase

B:
mRNA to Protein: Translation

leader  start codon  coding region  stop codon  tail

AUGNNN  UAG  3'

UACNN'N'  5'  5'

fMet  formyl  methionine

Translation

shift position

5' UAG  3'
THE SUGAR SUBUNIT OF DNA AND RNA

FISHER PROJECTION

D-(-)-glyceraldehyde

D-(-)-ribose

D-(+)-glyceraldehyde

2-deoxyribose
Nucleosides and Nucleotides

Nucleoside:

- adenosine
- cytidine
- guanosine
- uridine (RNA)
- thymidine (DNA)

Nucleotide monophosphate: NMP or dNMP

- adenylic acid
- cytidylic acid
- guanylic acid
- uradylic acid (RNA)

Cyclic Nucleotide

- 3',5'-cyclic AMP (cAMP)
- 2',3'-cyclic AMP

 NDP or dNDP

- thymidylic acid (DNA)

 NOTE: In DNA the OH in the brackets is absent

NTP or dNTP
**Structure and Nomenclature for dinucleotides and polymers**

\[
d\text{NpdNpdN} = d(\text{NpNpN}) = d(\text{NNN}) \text{ for oligodeoxyribonucleotides}
\]

\[
\text{NpNpN} = \text{NNN} \text{ for oligoribonucleotides}
\]

\[
d(\text{NNN})Nd(\text{NNN}) \text{ for mixed oligo ribo and deoxyribonucleotides}
\]

(Embedded substrates, such as embedded RNA)

When strands associate the two sequences are given, both in the 5'-3'
\[
d(\text{ACGTATG}) \cdot d(\text{CATACGT})
\]

**Polymers.**

\[
\text{poly (dA)} : \text{homopolymer } d(\text{AAA})n = d(\text{AAAAAAA}...) \\
\text{poly (dA-dT)} : \text{heteropolymer } d(\text{AT})n = d(\text{ATATATA}...) \\
\text{poly (dA,dT)} : \text{random copolymer } d(\text{ATTAATTTTATATTA}...)
\]

When polymer strands associate the stoichiometry is given:

\[
\text{poly (A) } \cdot 2 \text{ poly(U)}
\]
Mechanism for the acid hydrolysis of the glycosidic bond in DNA.

File: acidhyd.cwg

Table. Rate of hydrolysis of the bases at pH 1.
(Kochetkov and Budovskii 1972)

<table>
<thead>
<tr>
<th>nucleoside</th>
<th>rate (sec)</th>
</tr>
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<tbody>
<tr>
<td>dA</td>
<td>4.3</td>
</tr>
<tr>
<td>dG</td>
<td>8.3</td>
</tr>
<tr>
<td>dC</td>
<td>0.0011</td>
</tr>
<tr>
<td>dU</td>
<td>0.001</td>
</tr>
<tr>
<td>A</td>
<td>0.0036</td>
</tr>
<tr>
<td>G</td>
<td>0.0093</td>
</tr>
<tr>
<td>C</td>
<td>0.00001</td>
</tr>
<tr>
<td>U</td>
<td>0.00001</td>
</tr>
</tbody>
</table>
Mechanism of strand cleavage following glycosidic bond hydrolysis

In the presence of piperidine, the β-elimination reactions may take place through the enamine.
RNA strand cleavage under basic condition

Path A

Path B
Rates of Hydrolysis of RNA under basic and acidic conditions

**Table. Basic Hydrolysis of RNA.**

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Conditions</th>
<th>Time</th>
<th>Temperature</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>ApA</td>
<td>0.5 N NaOH</td>
<td>8 h</td>
<td>28ºC</td>
<td>47% hydrolysis</td>
</tr>
<tr>
<td>RNA</td>
<td>0.1 N NaOH</td>
<td>20 min</td>
<td>100ºC</td>
<td>mononucleotides</td>
</tr>
<tr>
<td>RNA</td>
<td>10% piperidine</td>
<td>90 min</td>
<td>100ºC</td>
<td>mononucleotides</td>
</tr>
<tr>
<td>RNA</td>
<td>1.0 N NaOH</td>
<td>0.7 min</td>
<td>27ºC</td>
<td>1% cleavage</td>
</tr>
<tr>
<td>RNA</td>
<td>pH 9</td>
<td>30 min</td>
<td>70ºC</td>
<td>1% cleavage</td>
</tr>
</tbody>
</table>

**Table. Acidic Hydrolysis of RNA.**

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Conditions</th>
<th>Time</th>
<th>Temperature</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>ApA</td>
<td>0.3 N HCl</td>
<td>8 h</td>
<td>45ºC</td>
<td>69% hydrolysis</td>
</tr>
<tr>
<td>RNA</td>
<td>pH 1</td>
<td>100 min</td>
<td>20ºC</td>
<td>10% cleavage</td>
</tr>
<tr>
<td>RNA</td>
<td>pH 2</td>
<td>4 min</td>
<td>100 ºC</td>
<td>10% cleavage</td>
</tr>
<tr>
<td>RNA</td>
<td>pH 3</td>
<td>40 min</td>
<td>100 ºC</td>
<td>10% cleavage</td>
</tr>
</tbody>
</table>
Basic Constituents of Nucleic Acids

THE BASES

Purines

Pyrimidines

The Four Letter Code: A, C, G, T
where A recognizes T and C recognizes G

guanine  
Gua  

adenine  
Ado  
thymine  
Thy

Bases are shown in their Watson Crick base-pairing arrangement
Minor RNA nucleosides, adenine derivatives

$m^1A$

$m^2A$

$m^6A$ (dm$^6A$ in DNA)

$i^6A$

$ms^2t^6A$

$t^6A$

$N^+$

Am

I

$m^1I$
Minor RNA nucleosides, cytosine derivatives

$m^3C$

$m^5C$

$s^2C$

(dm$^5C$ in DNA)

$ac^4C$

$s^2m^5C$

Cm

(DNA only, R=H or a sugar, found in T even bacteriophages)
Minor RNA nucleosides, guanine derivatives

\[
\begin{align*}
\text{m}^1\text{G} & \quad (\text{dm}^1\text{G in DNA}) \\
\text{m}^2\text{G} & \\
\text{m}^2_2\text{G} & \quad (\text{dm}^2_2\text{G in DNA}) \\
\text{m}^7\text{G} & \quad (\text{dm}^7\text{G in DNA}) \\
\text{Gm} & \\
\text{Y} & 
\end{align*}
\]
Minor RNA nucleosides, Uracil derivatives

- D or hU
- m^3U (found in DNA of SP 8 bacteriophage)
- rT or T
- cm^5U R=H, cmm^5U, R=CH_3
- s^2cm^5U R=H, s^2am^5U, R=CH_3
- s^2m^5U
- s^2U
- s^2mam^5U
- X
- Um
- Y or YU
Localization of lone pairs in bases.

In plane lone pairs, $\sigma$ type

out of plane lone pairs, $p$ type conjugated to $\pi$ system
ACID-BASE PROPERTIES

腺嘌呤 (pKa = 3.5)  | 胞嘧啶 (pKa = 4.2)  | 胞嘧啶 (pKa = 9.4)  | 胞嘧啶 (pKa = 9.7)  | 胞嘧啶 (pKa = 9.3)

磷酸二酯键的酸碱平衡常数（pKa）

- pKa = 1
- pKa = 7
TAUTOMERS OF THE BASES

- Amino
- Imino
- Imino
- Imino
- Imino/keto
- Imino/keto
- Imino/enol
- Keto
- Enol
- Keto
- Keto
- Enol
- Enol

etc
## Base Pairing Combinations

<table>
<thead>
<tr>
<th></th>
<th></th>
<th>No.</th>
<th>Figure</th>
</tr>
</thead>
<tbody>
<tr>
<td>homo purine</td>
<td></td>
<td>7</td>
<td>homops1.cw2</td>
</tr>
<tr>
<td>homo pyrimidine</td>
<td></td>
<td>5</td>
<td>homopy1.cw2</td>
</tr>
<tr>
<td>hetero purine</td>
<td></td>
<td>4</td>
<td>hetpu1.cw2</td>
</tr>
<tr>
<td>hetero pyrimidine</td>
<td></td>
<td>1</td>
<td>homopy1.cw2</td>
</tr>
<tr>
<td>purine-pyrimidine</td>
<td>AT</td>
<td>4</td>
<td>pupybp1.cw2</td>
</tr>
<tr>
<td>purine-pyrimidine</td>
<td>GC</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td>23</td>
<td></td>
</tr>
</tbody>
</table>
Base pairing schemes for identical purines

homo purine - symmetric

1

2

3

4

homo purine - asymmetric

5

6

anti

Hoogsteen

Reverse Hoogsteen

anti
Base pairing schemes for pyrimidines

homo pyrimidine, symmetric

homo pyrimidine, asymmetric

hetero pyrimidine, symmetric

anti

anti
Base Pairing Schemes for mixed purines

hetero purine symmetric

8

9

10

11

heteropurine - asymmetric

anti
Purine-Pyrimididine Base Pairs

Pseudosymmetric, Watson-Crick Base Pair

Reversed Watson-Crick, asymmetric

Hoogsteen

Reversed Hoogsteen

Purine-Pyrimidine Base Pairs

anti
Conformational Analysis of Nucleosides and Nucleotides
Definition of Angles in Nucleotides

\[ \alpha \]
\[ \beta \]
\[ \gamma \]
\[ \delta \]
\[ \epsilon \]
\[ \zeta \]

Pyrimidines

\[ \chi \]

Purines

\[ \chi \]
Definition of the bond angles in deoxyribose ring system and the pseudorotation equation

The torsion bonds are defined by the sugar ring atoms. Example, $\tau_1$ is defined by O4'-C1'-C2'-C3'.

**Pseudorotation equation:**

$$\tau_i = \tau_{\text{max}} \cdot \cos(P + 144 \cdot (i + 3))$$

where $P$ is the phase angle
Definition of envelope and twist forms of deoxyribose ring system

Envelope form

- 4 atoms in plane
- 1 atom out of plane (#5)

Twist Form

- 3 atoms in plane
- 1 atom below plane (#4)
- 1 atom above plane (#5)

C2'-endo
2E

C2'-exo
2E

C2'-endo, C3'-exo
\(\frac{2}{3}T\)

C2'-exo, C3'-endo
\(\frac{3}{2}T\)

P=162
P=342
P=180
P=0
Pseudorotation Cycle for Ribose Ring
Potential Energy Surface for the Deoxyribose Ring System as a function of $\tau$ and $P$.

$$E = \text{kcal, perpendicular to plane of paper}$$
Origin of the high energy of the O4'-exo conformation of deoxyribonucleosides

Bad VDW interaction due to eclipsed bond

Bad VDW interaction
Glycosyl Bond Angle Terms

Anomeric effect in phosphodiesterstors explains preference for gauche conformations
A & B duplex DNA
DIFFERENT PERSPECTIVES ON THE WATSON CRICK BASE PAIR (BP)

TOP VIEW

MAJOR GROOVE SIDE

C$_2$ pseudo axis of symmetry

minor groove side

SIDE VIEW

Looking into minor groove

SCHEMATIC VIEW

\[ \text{5'} - \text{G} - 3' \]

\[ \text{3'} - \text{C} - 5' \]