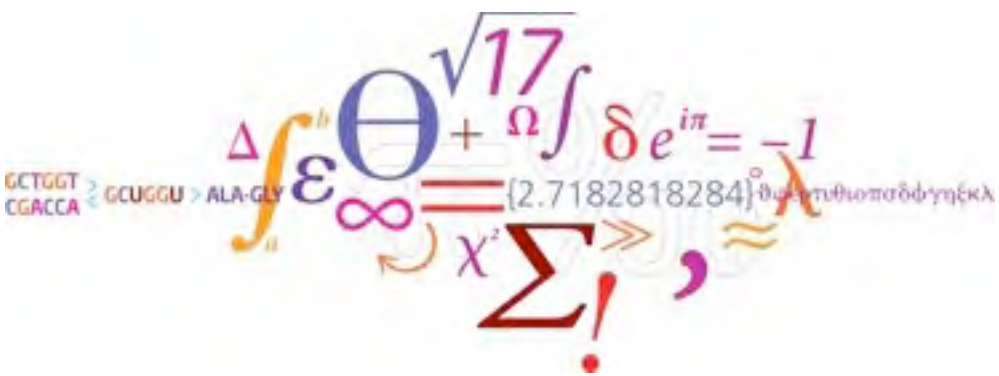
Comparative Genomics

Introduction to DNA atlases

(DNA structures)



Dave Ussery

Genomics of Prokaryotes Workshop
Universidad Miguel Hernández
Alicante, Spain

Monday, 12 December, 2011

Center for Biological Sequence Analysis
Department of Systems Biology

Monday, 12 December, 2011

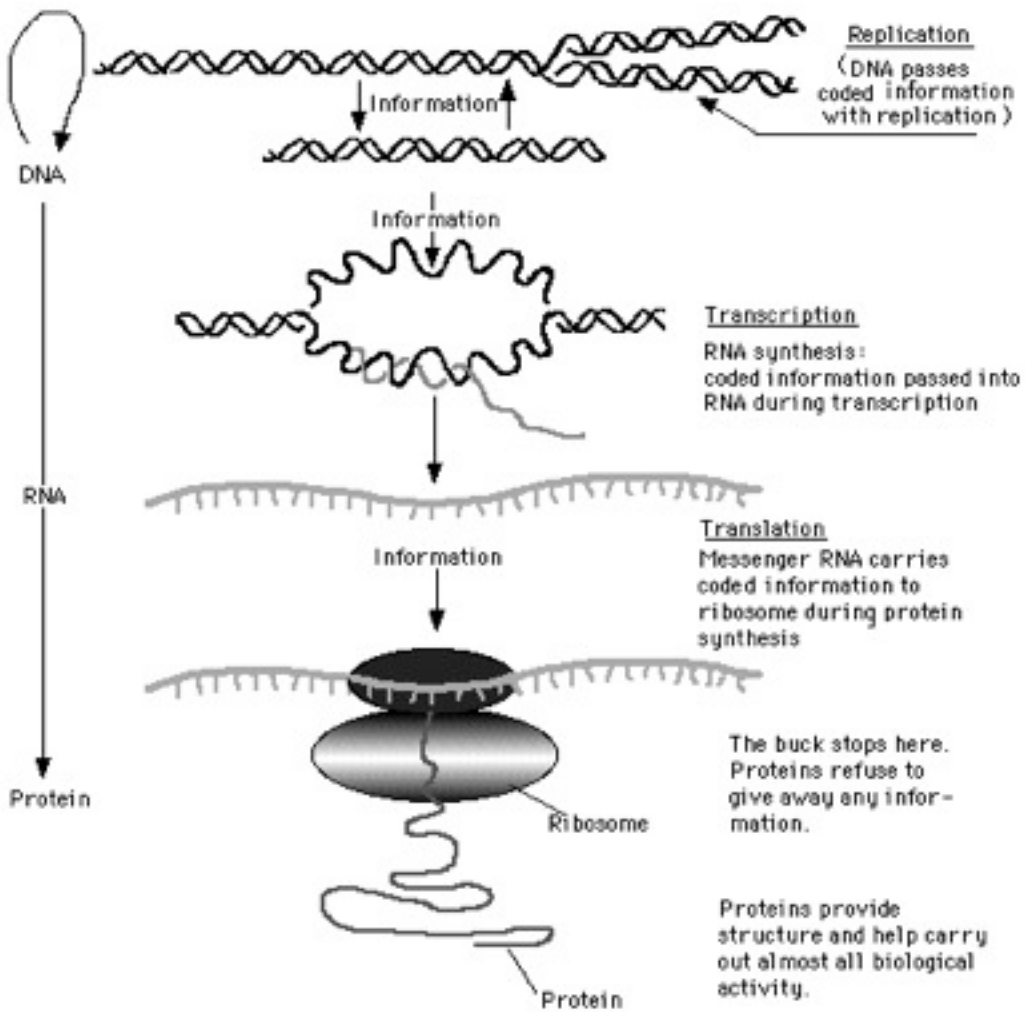
THE OXFORD ENGLISH DICTIONARY

bioinformatics, n.

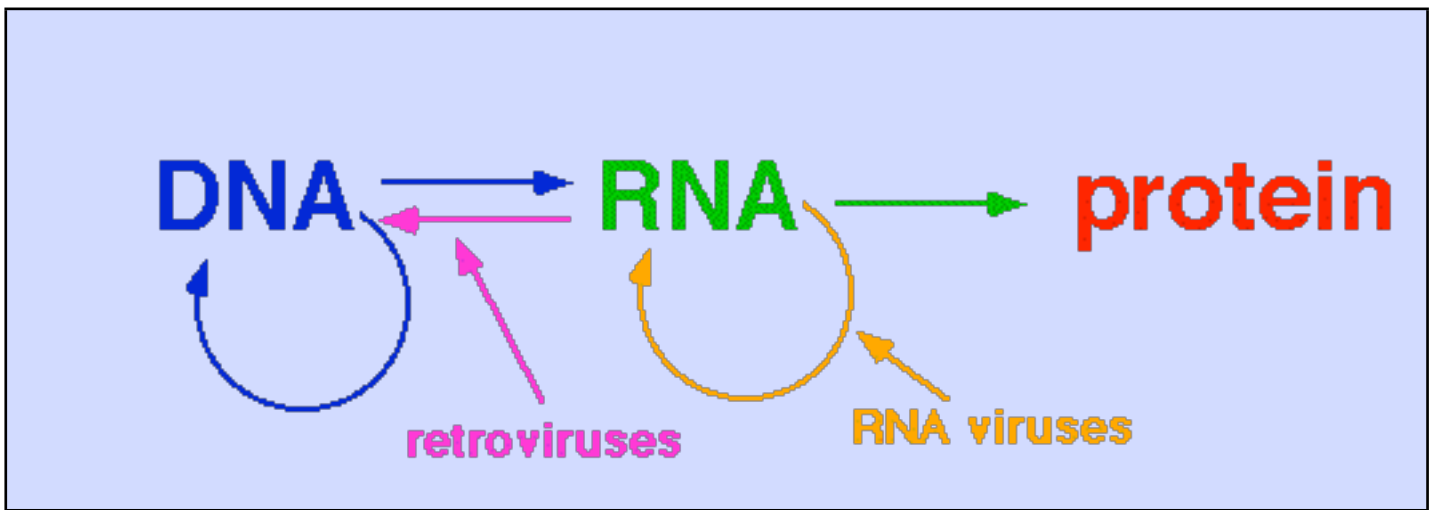
The science of information and information flow in biological systems, esp. the use of computational methods in genetics and genomics.

1978 P. HOGEWEG in *Simulation* **31** 90/1 Since 1970 she has been a staff member at the Subfaculty of Biology of the University of Utrecht, with her main field of research in bioinformatics. **1985** *Jrnl. Theoret. Biol.* **113** 719 (*heading*) Tumor escape from immune elimination... R. J. De Beer, Bioinformatics Group, University of Utrecht. **1986** *Philos. Trans. Royal Soc.* A. **317** 324 The area of modelling mutants from a known structure has been revolutionized by the latest tools of molecular graphics... This is a key element in the whole technology and has attracted much interest (for example, the recent E.E.C. 'Bioinformatics' programme). **1987** *Science* 4 Sept. 1108/3 One of the latest developments [at the European Molecular Biology Laboratory] has been the creation of a new research program in bioinformatics. This is intended to bring together research in computing science, structural biology, and molecular genetics. **1996** *Fast Company* Aug.-Sept. 32/3 A lot of breakthroughs in medicine will come out of the efforts of bio-informatics. **2001** *N.Y. Times* 4 Jan. B6/2 The hope..is to make New York a leader in cutting-edge fields like bioinformatics, in which computers are used to decipher genes and proteins.

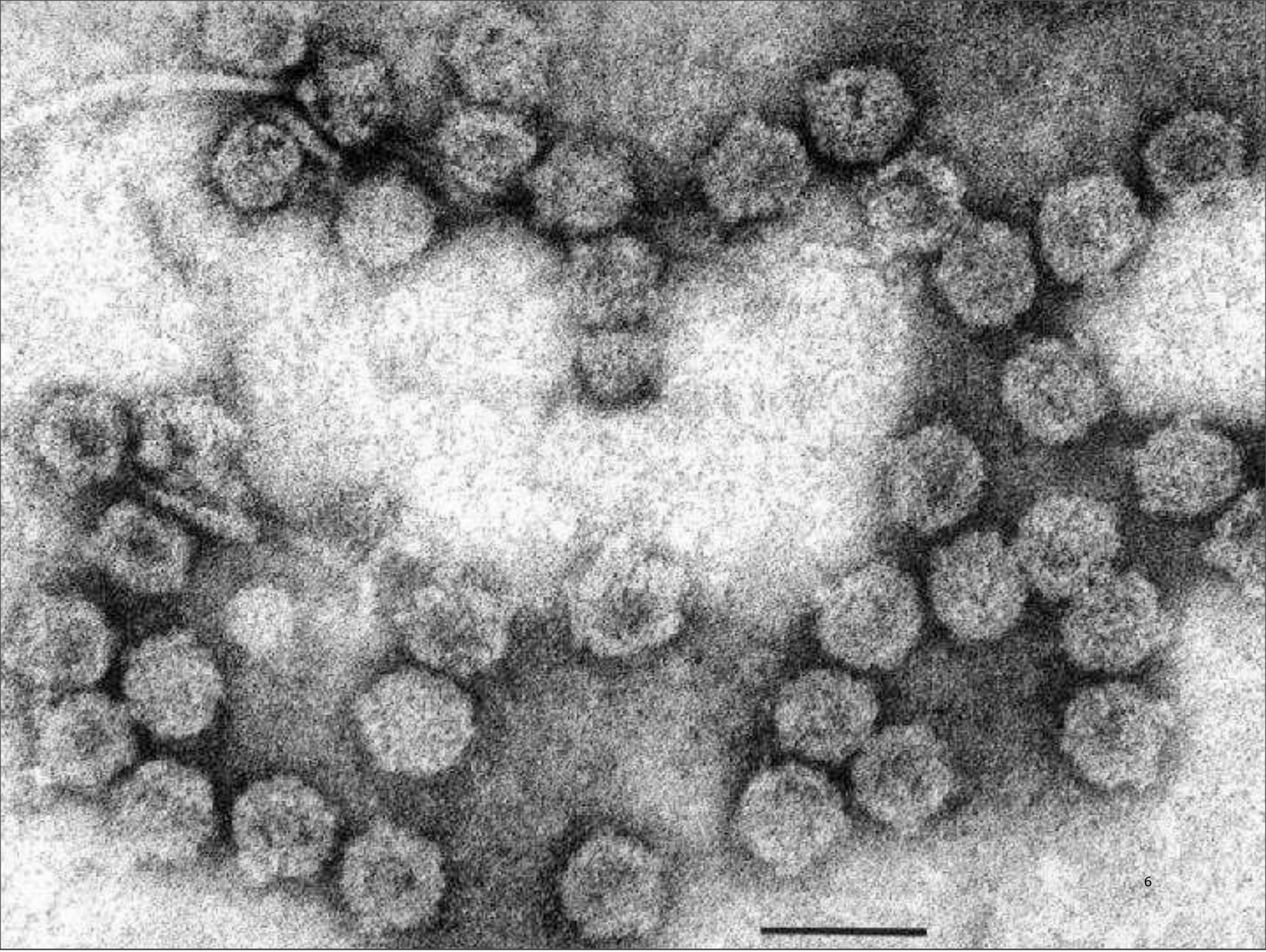
The Central Dogma of Molecular Biology



What is Biological Information?



Genome -> Transcriptome ->Proteome



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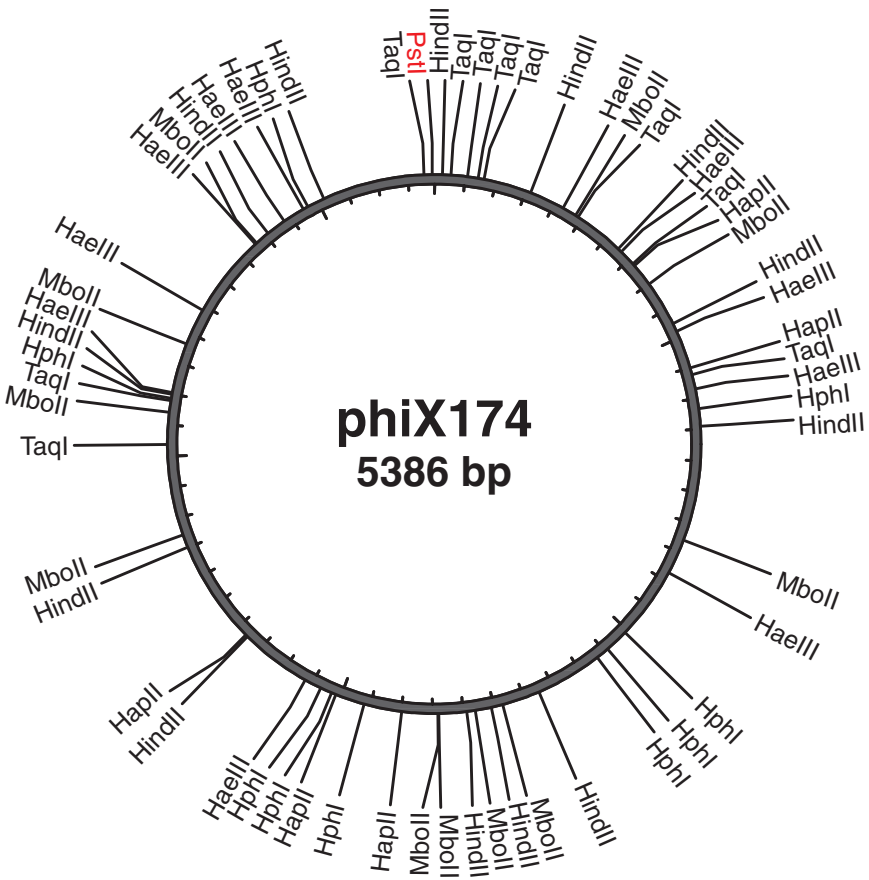
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PstI
HindII
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HindII
HaeIII
TaqI
HapII
MboII
HindII
HaeIII
HapII
TaqI
HaeIII
HphI
HindII
MboII
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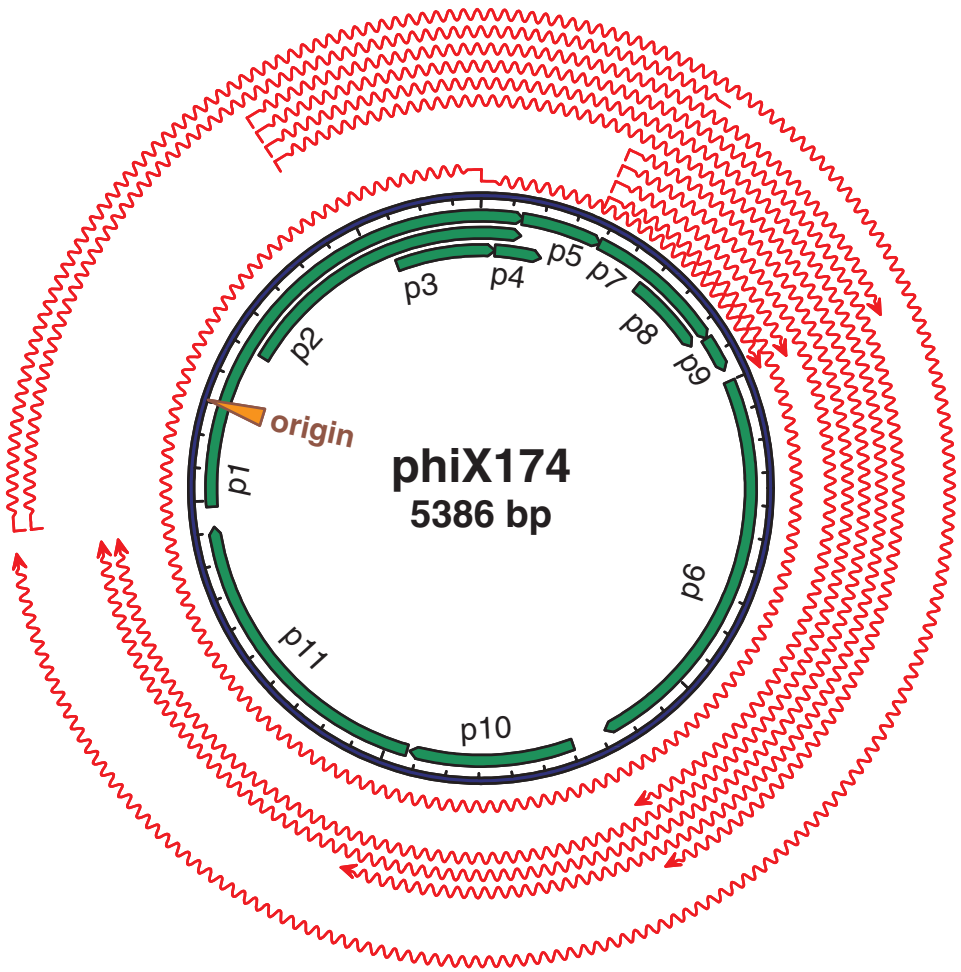
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5386 bp
origin
p1
p2
p3
p4
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p7
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p9
p6
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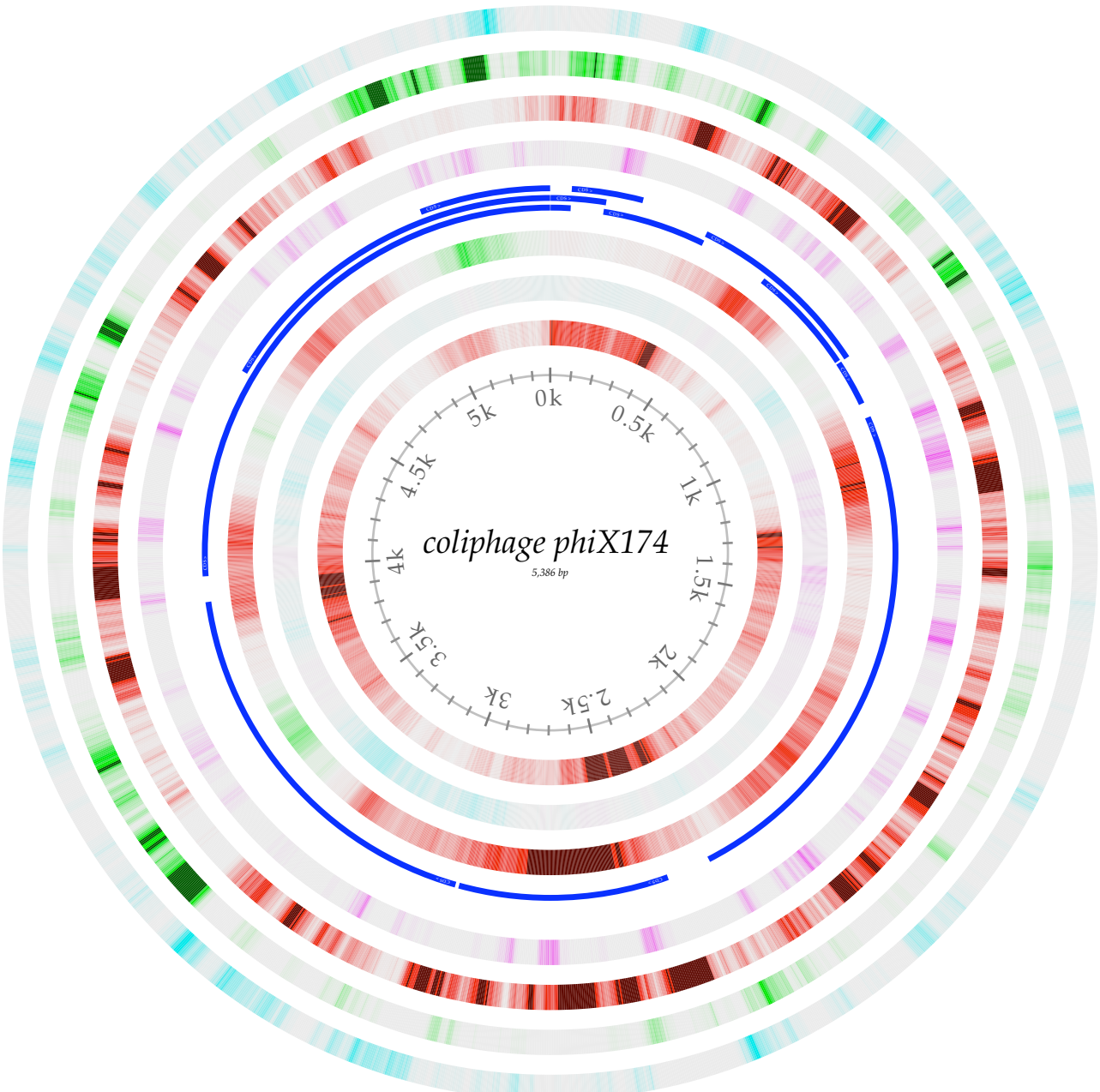
p11



G Content
fix avg
0.00 0.40

A Content
fix avg
0.00 0.40

T Content
fix avg
0.00 0.40

C Content
fix avg
0.00 0.40

Annotations:
CDS +

AT Skew
fix avg
-0.20 0.20

GC Skew
fix avg
-0.20 0.20

Percent AT
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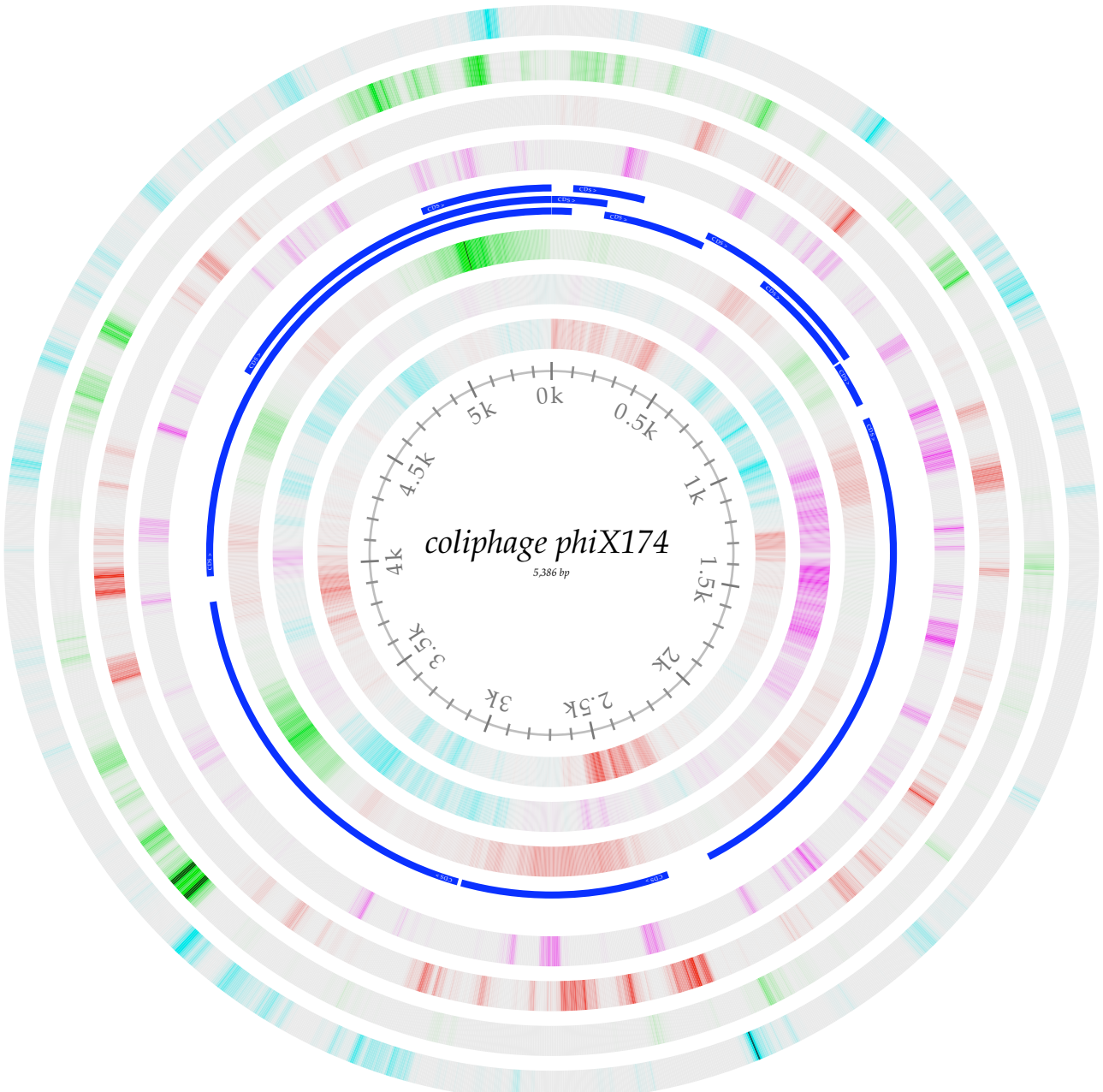
Resolution: 3



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A Content
dev avg
0.01 0.47

T Content
dev avg
0.10 0.53

C Content
dev avg
0.04 0.39

Annotations:
CDS +

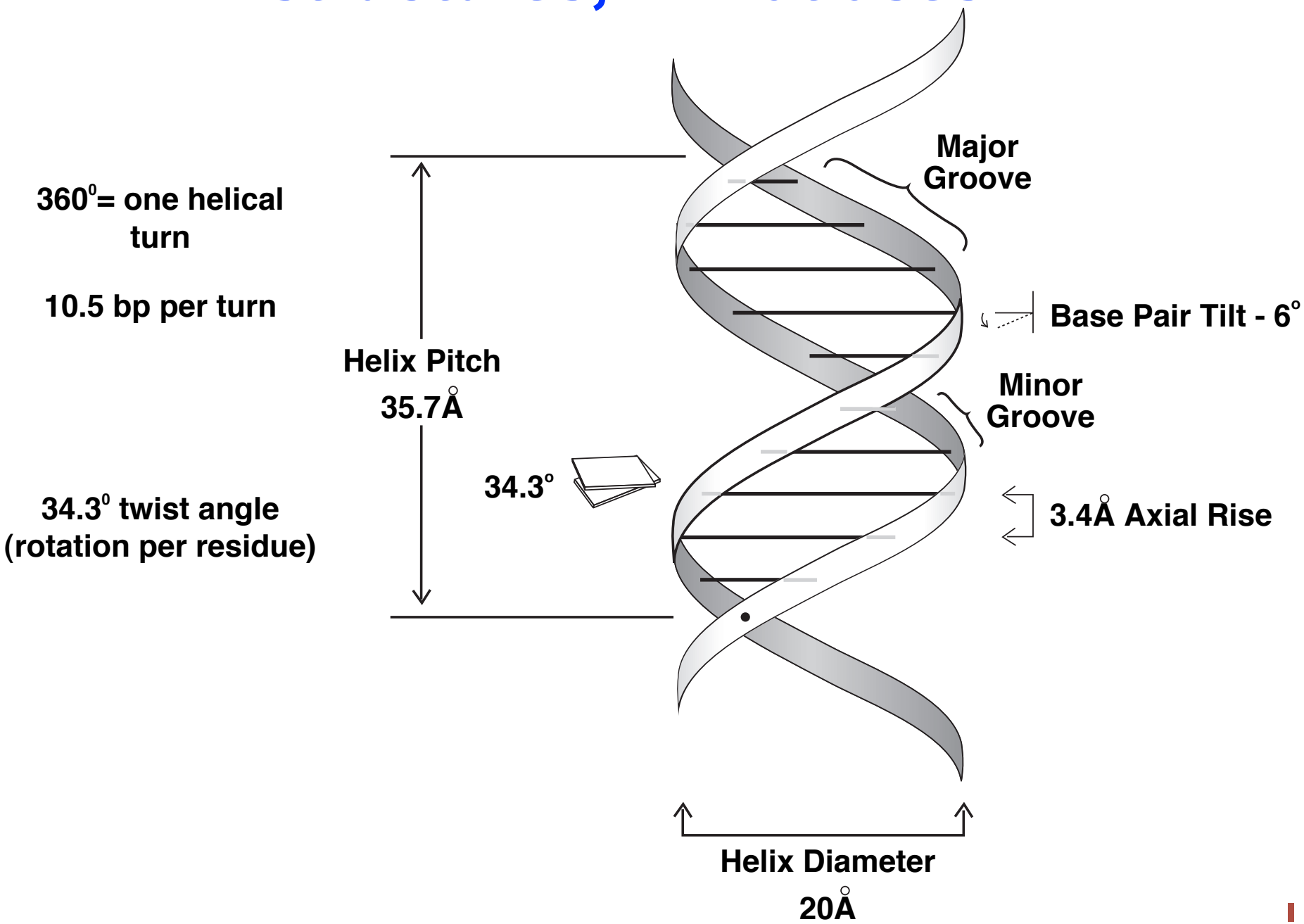
AT Skew
dev avg
-0.33 0.18

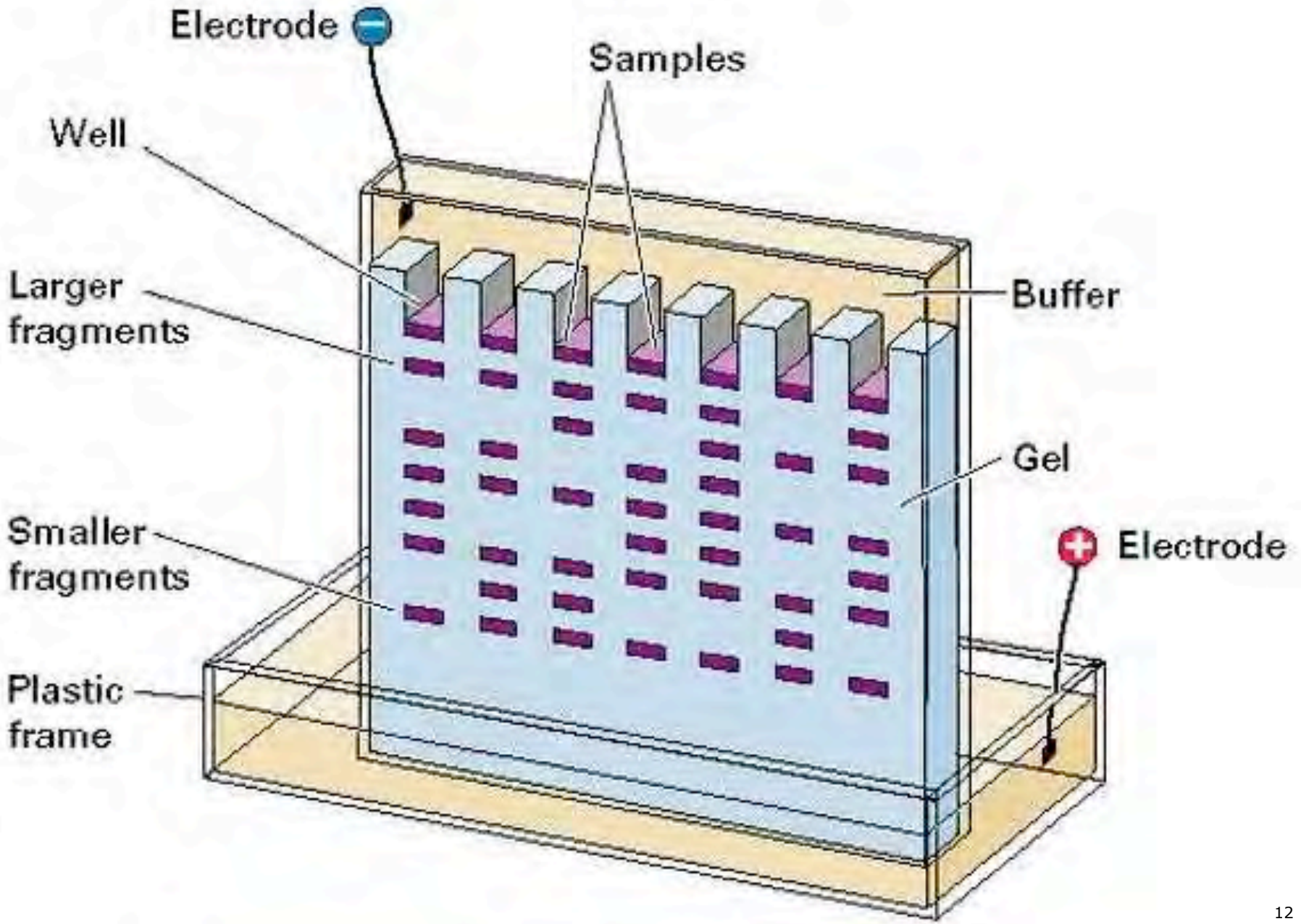
GC Skew
dev avg
-0.10 0.14

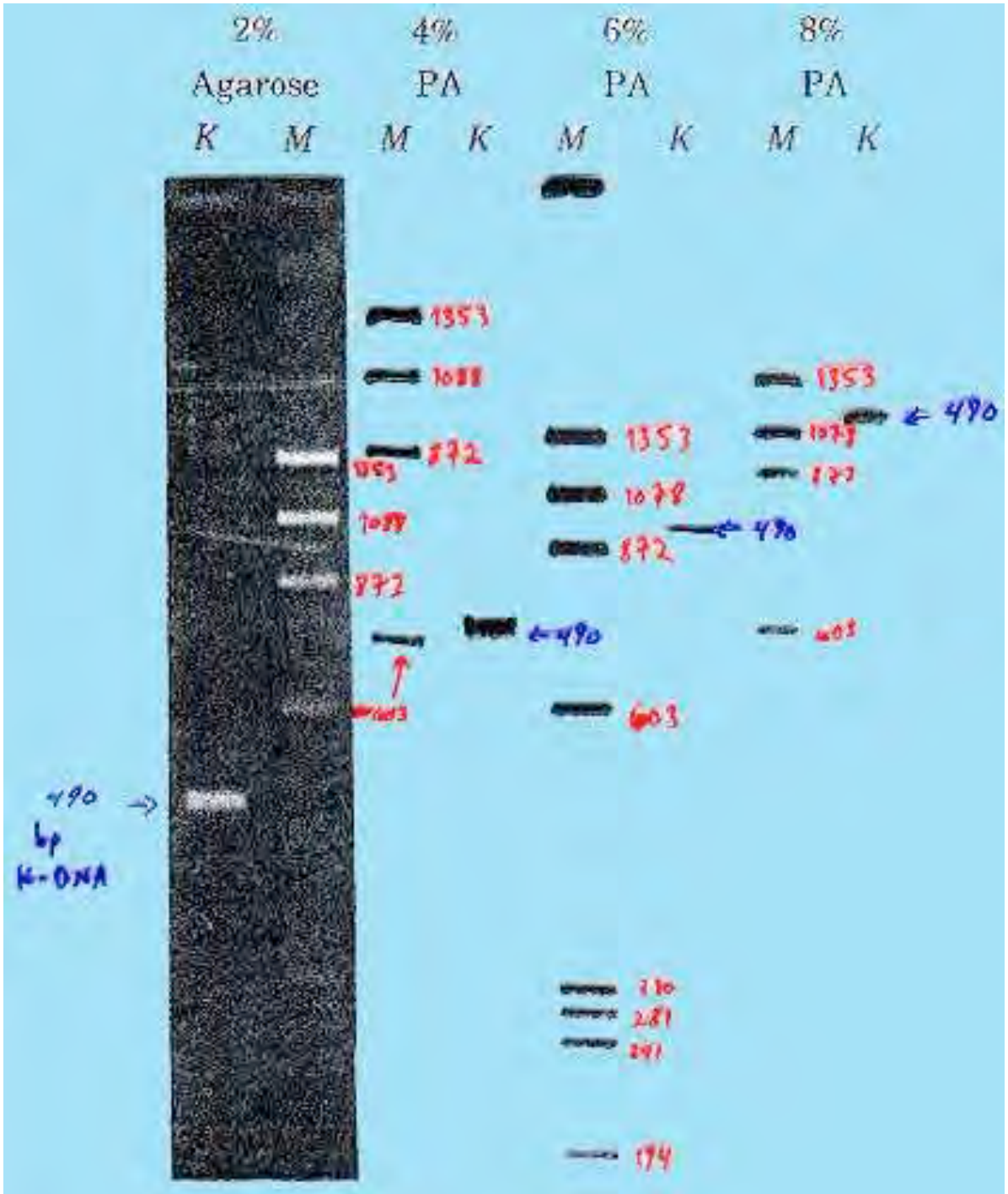
Percent AT
dev avg
0.47 0.63

Resolution: 3

a digression - a few words about DNA structures, DNAatlases....




Electrode
Samples
Well
Larger fragments
Buffer
Gel
Smaller fragments
Electrode
Plastic frame


2%
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4%
PA
6%
PA
8%
PA
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M
M
K
M
K
M
K
1353
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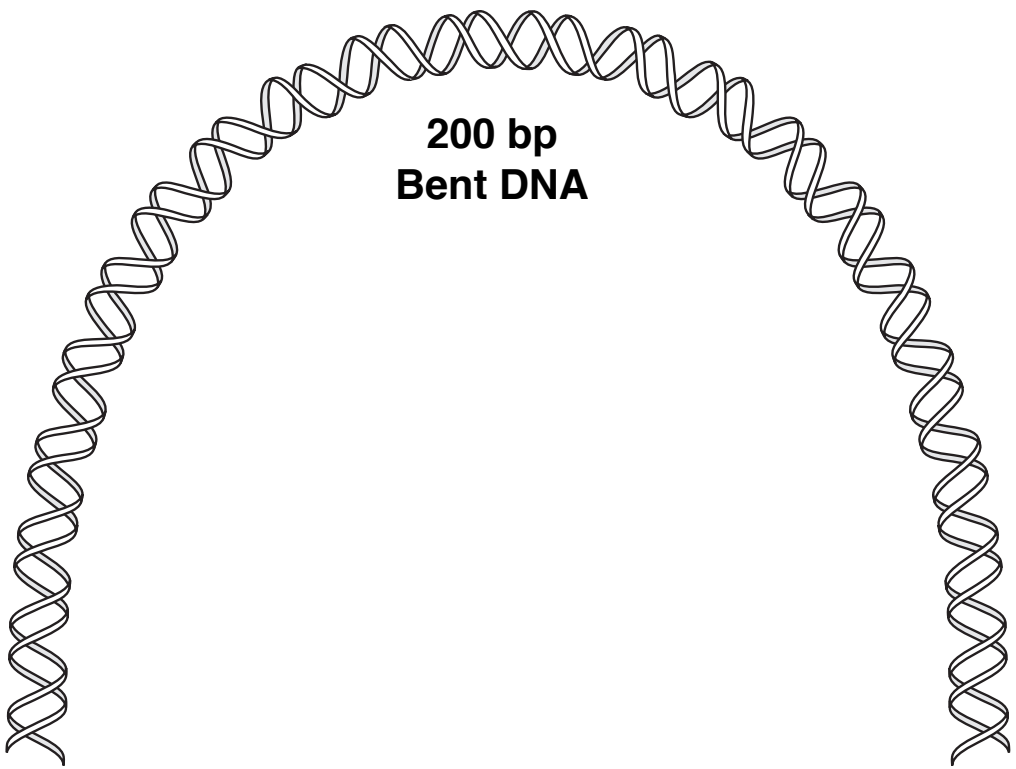
603
1078
872
603
490
1353
1078
872
603
490
490
bp
λ-DNA
310
281
271
194

A.

200 bp
Straight DNA

B.



200 bp
Bent DNA

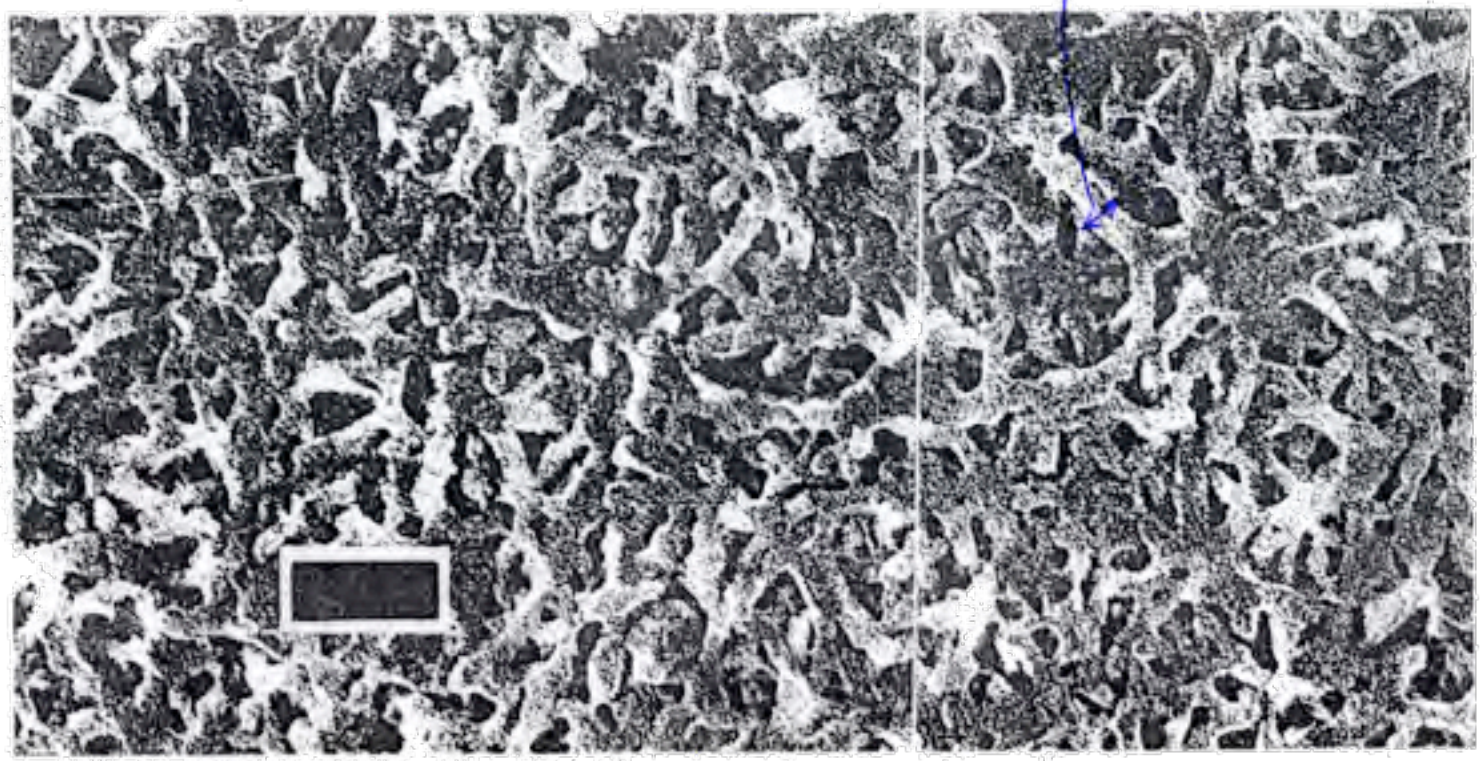
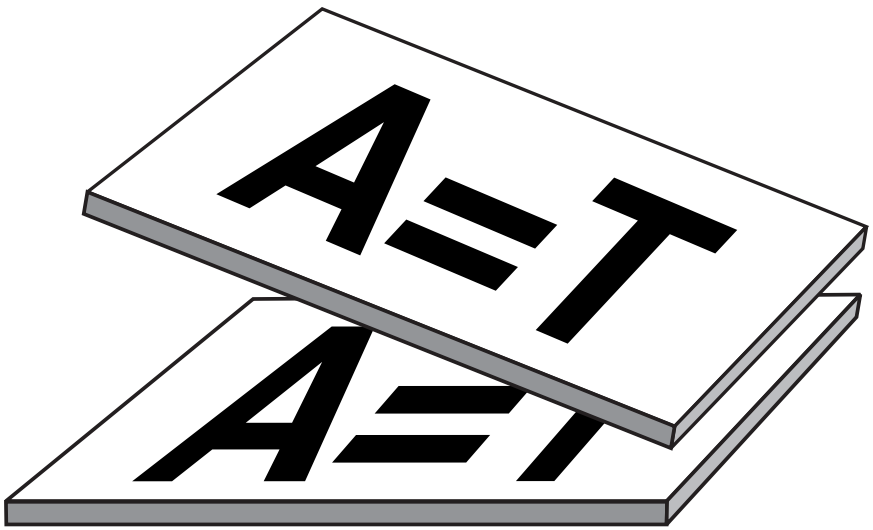


Figure 8.10 Electron micrograph of a portion of a 2% agarose gel, 1 μm × 0.5 μm overall: small black rectangle is 1000 Å × 500 Å. Individual gel fibers are about 100 Å wide. Courtesy of Sue Whytock and John Finch.



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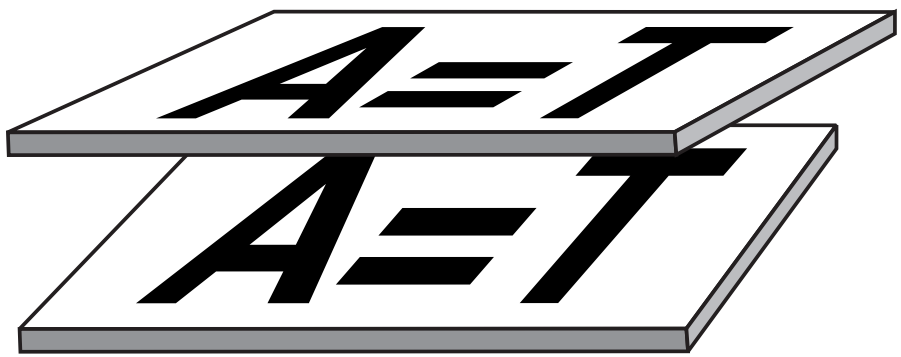
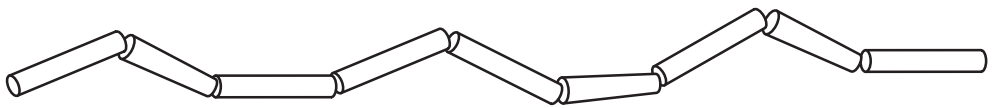
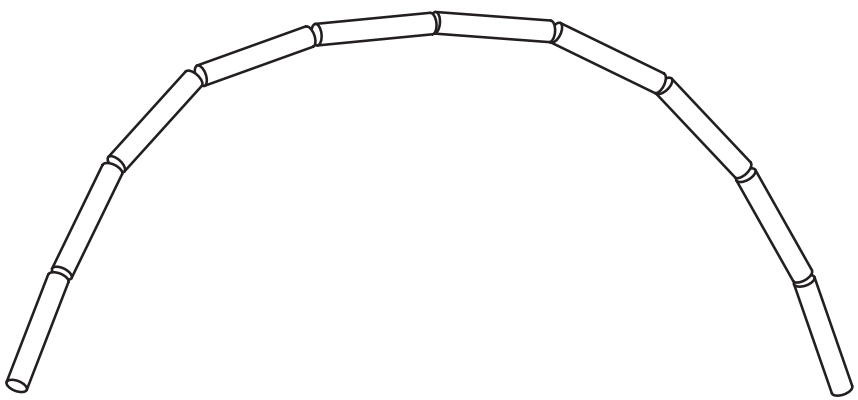


Roll

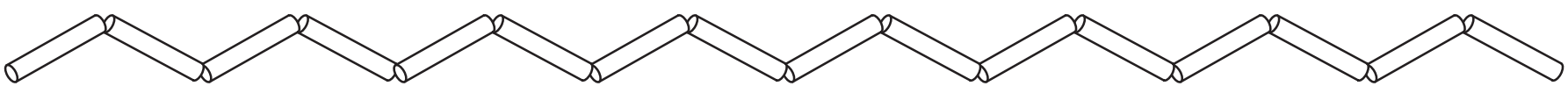
Random Bends



Bends Phased at 10.5 bp



Bends Phased at 16 bp



1 11 21 31 41

. . . . .

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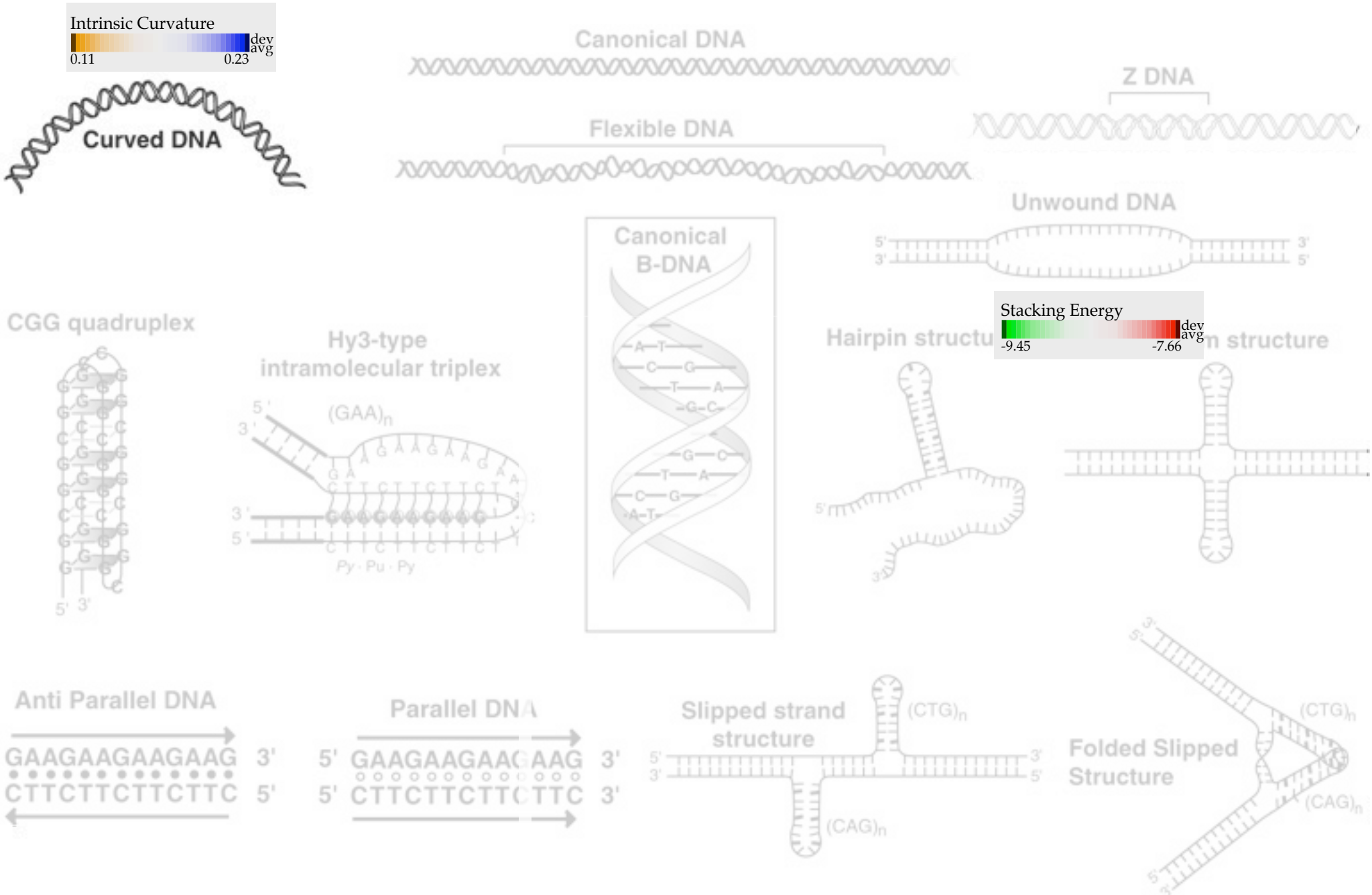
Intrinsic Curvature
dev
avg
0.11
0.23
Curved DNA
Canonical DNA
Z DNA
Flexible DNA
Unwound DNA
Canonical
B-DNA
Stacking Energy
dev
avg
-9.45
-7.66
CGG quadruplex
Hy3-type
intramolecular triplex
Hairpin structu
n structure
Anti Parallel DNA
5' GAAGAAGAAGAAG 3'
3' CTTCTTCTTCTTC 5'
Parallel DNA
5' GAAGAAGAAGAAG 3'
5' CTTCTTCTTCTTC 3'
Slipped strand
structure
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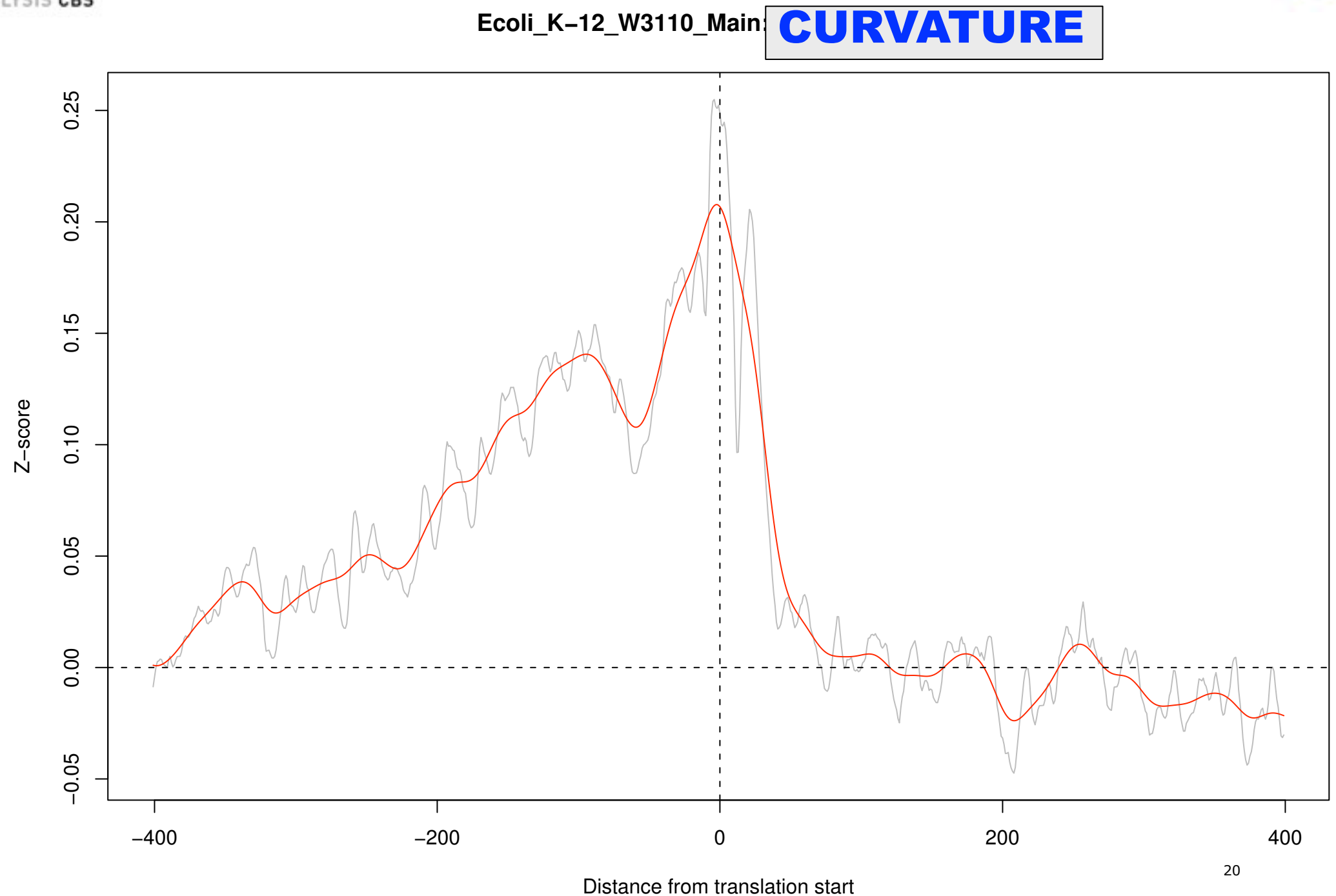
(CAG)n
Folded Slipped
Structure
(CTG)n
(CAG)n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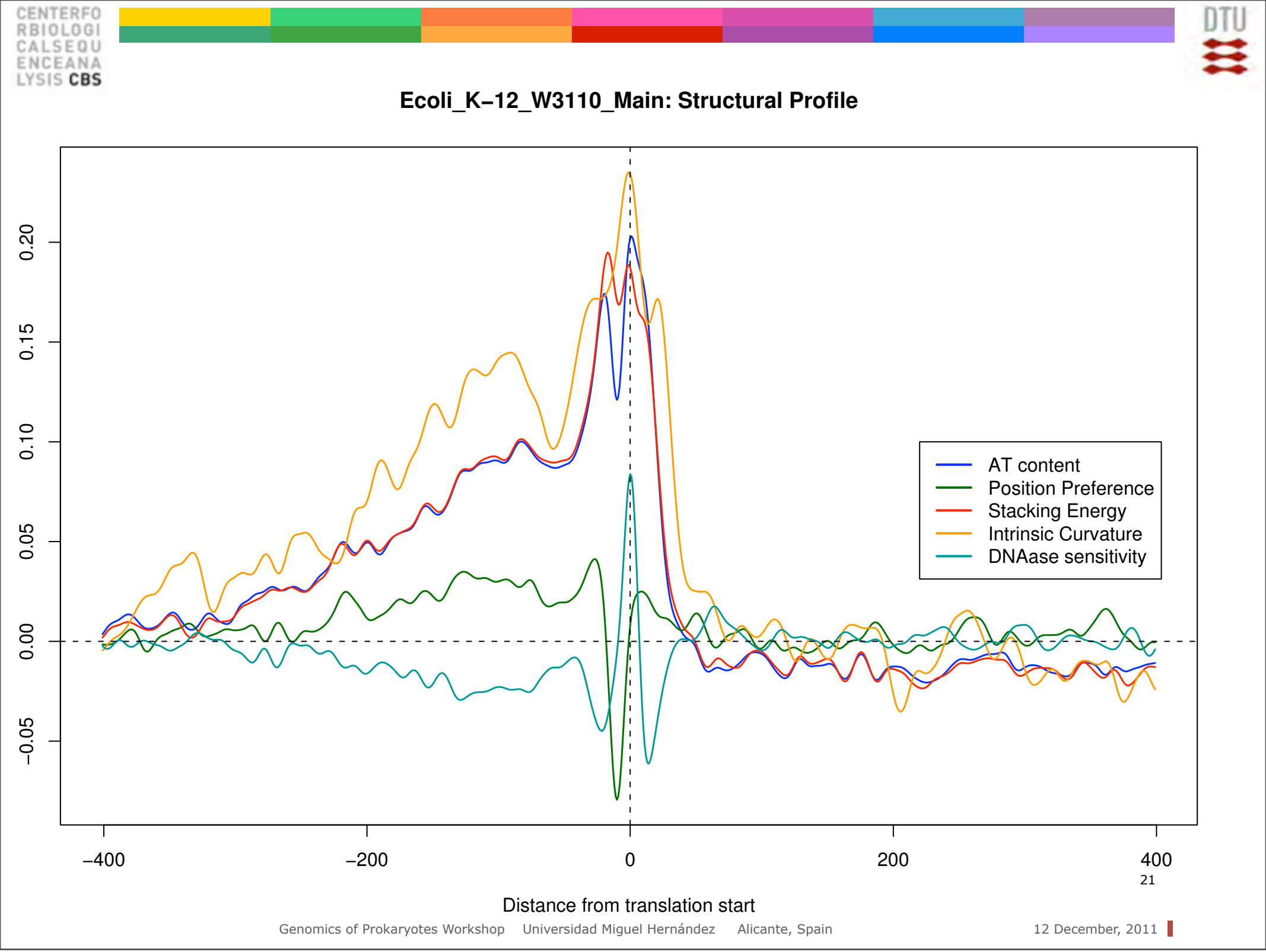
0
200
400
Distance from translation start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AT content
Position Preference
Stacking Energy
Intrinsic Curvature
DNAase sensitivity
−400
−200
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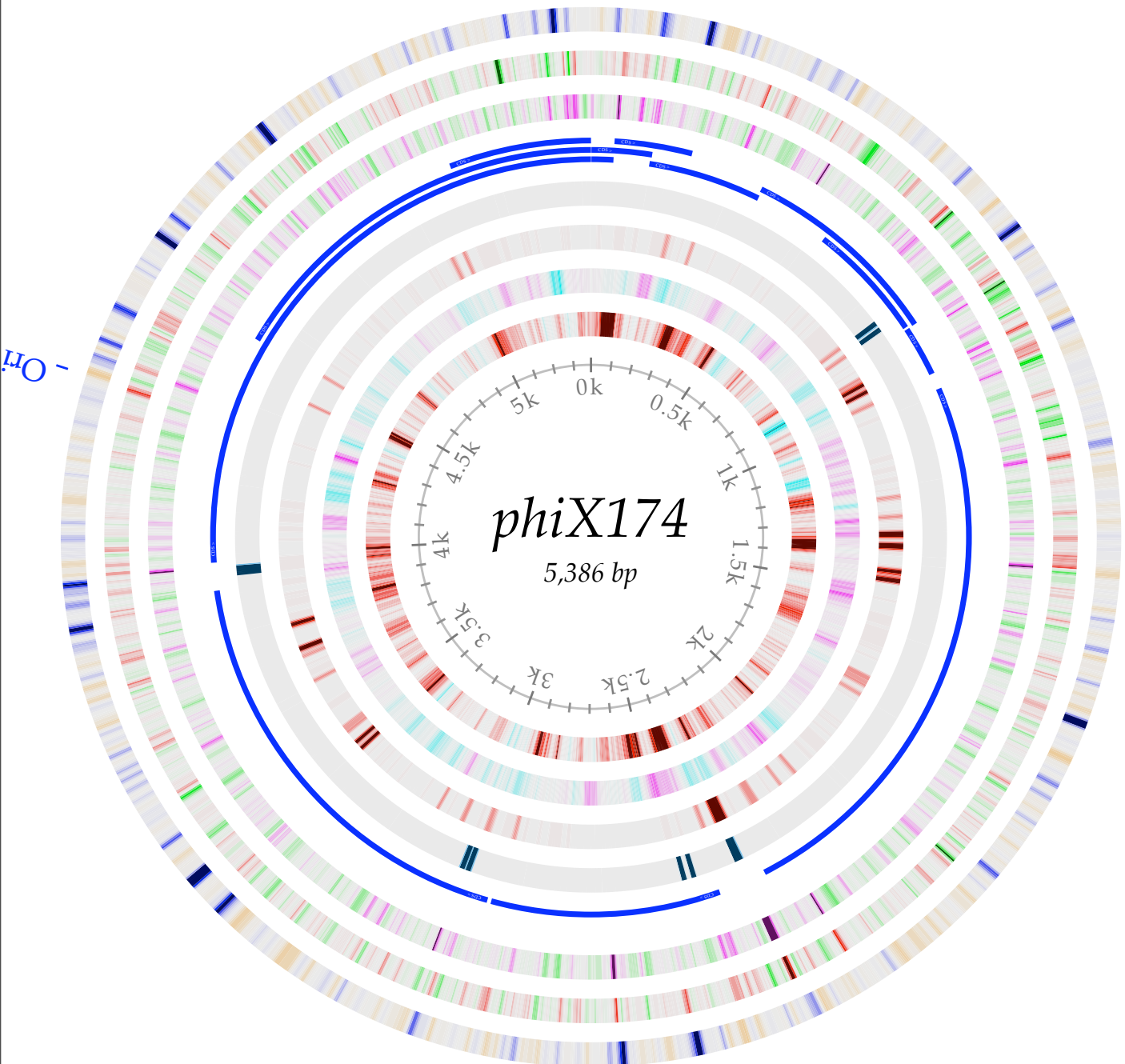
200
400
Distance from translation start



Intrinsic Curvature

-0.09 0.51

Stacking Energy

-10.31 -5.40

Position Preference

0.03 0.25

Annotations:

CDS +

CDS -

Perfect-palindromes

-0.25 0.28

Inverted Repeats

3.54 7.83

GC Skew

-0.25 0.29

Percent AT

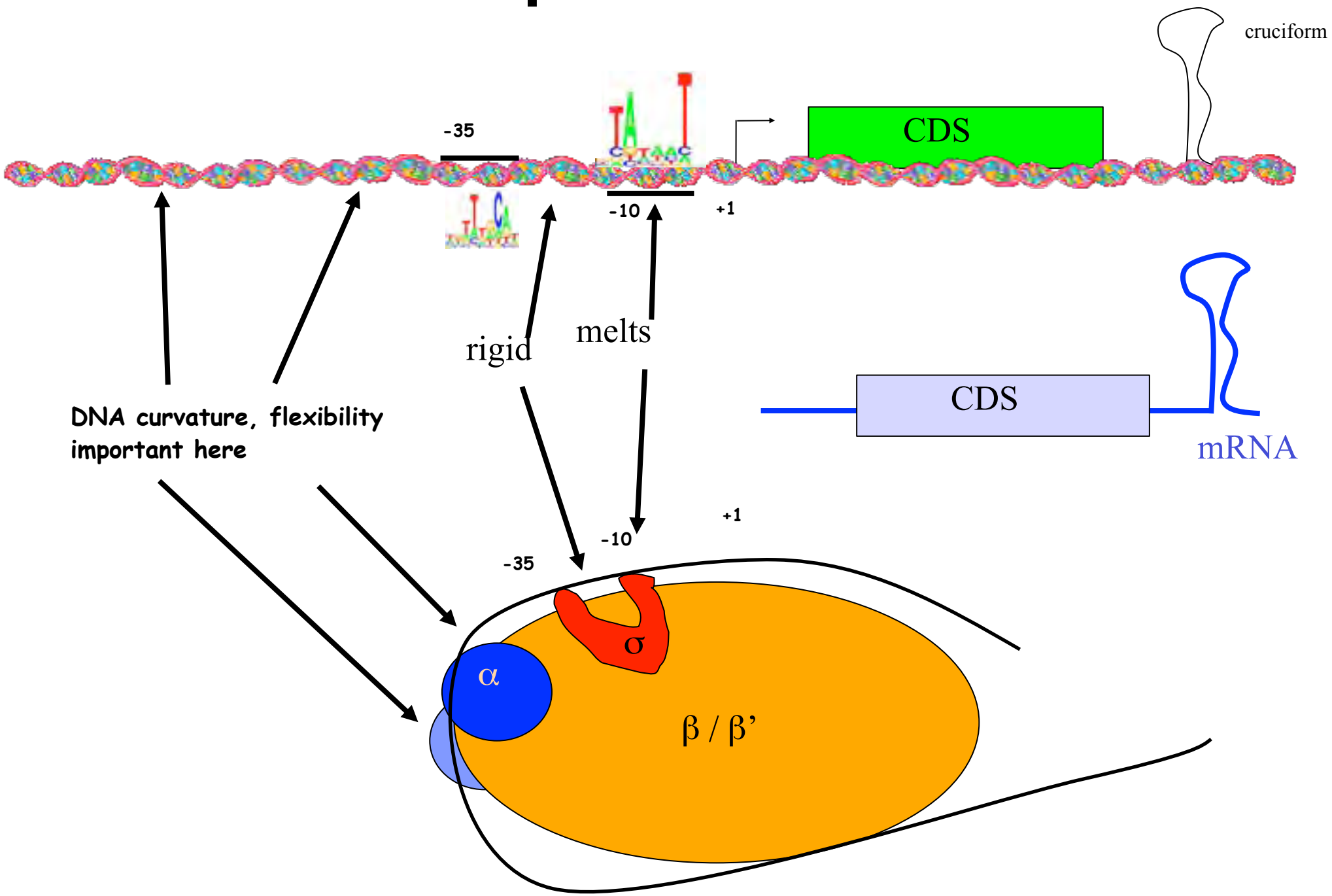
0.35 0.65

Resolution: 3

http://www.cbs.dtu.dk/
Center for Biological Sequence Ar

GENOME ATLAS

Promoter Structural profile



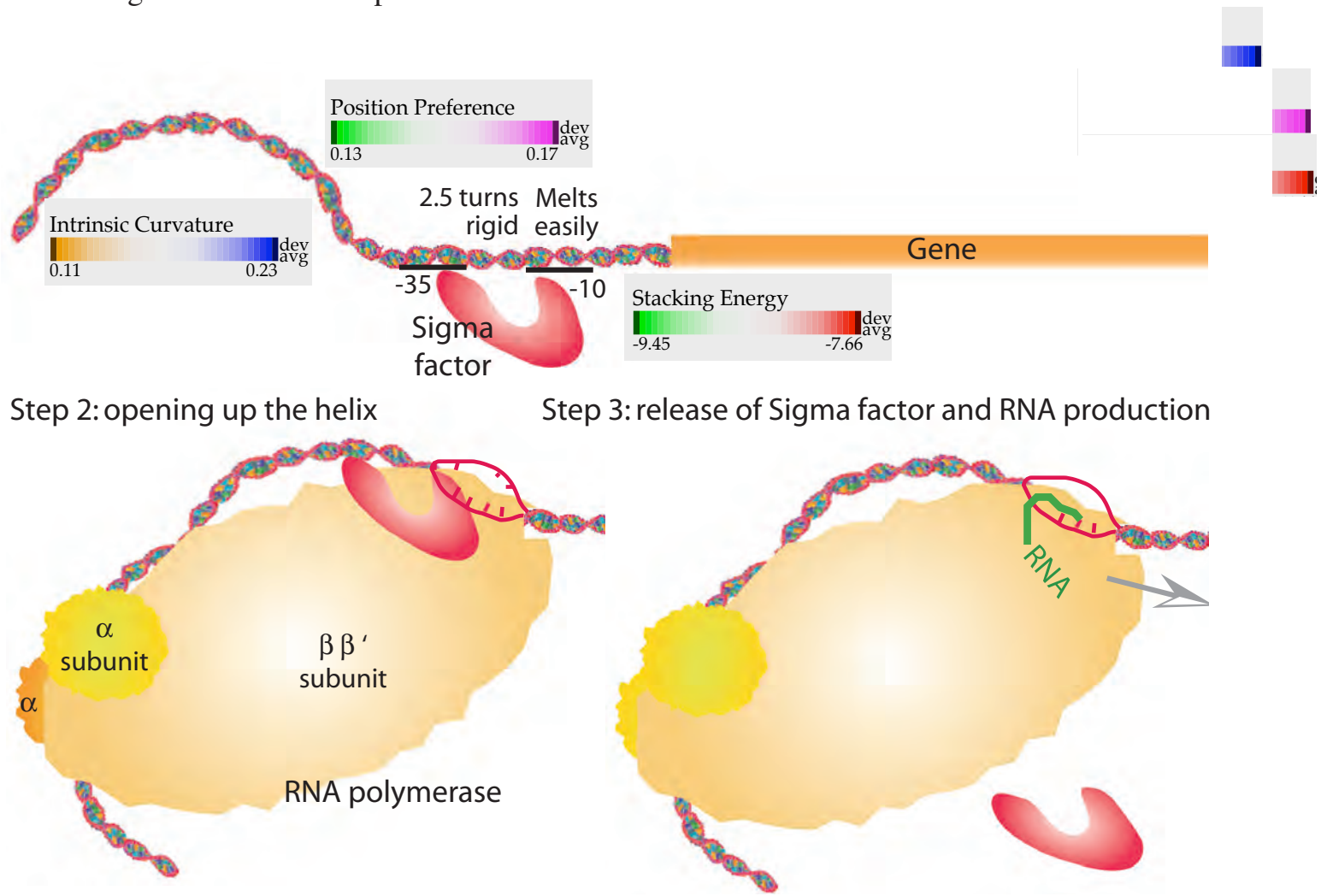
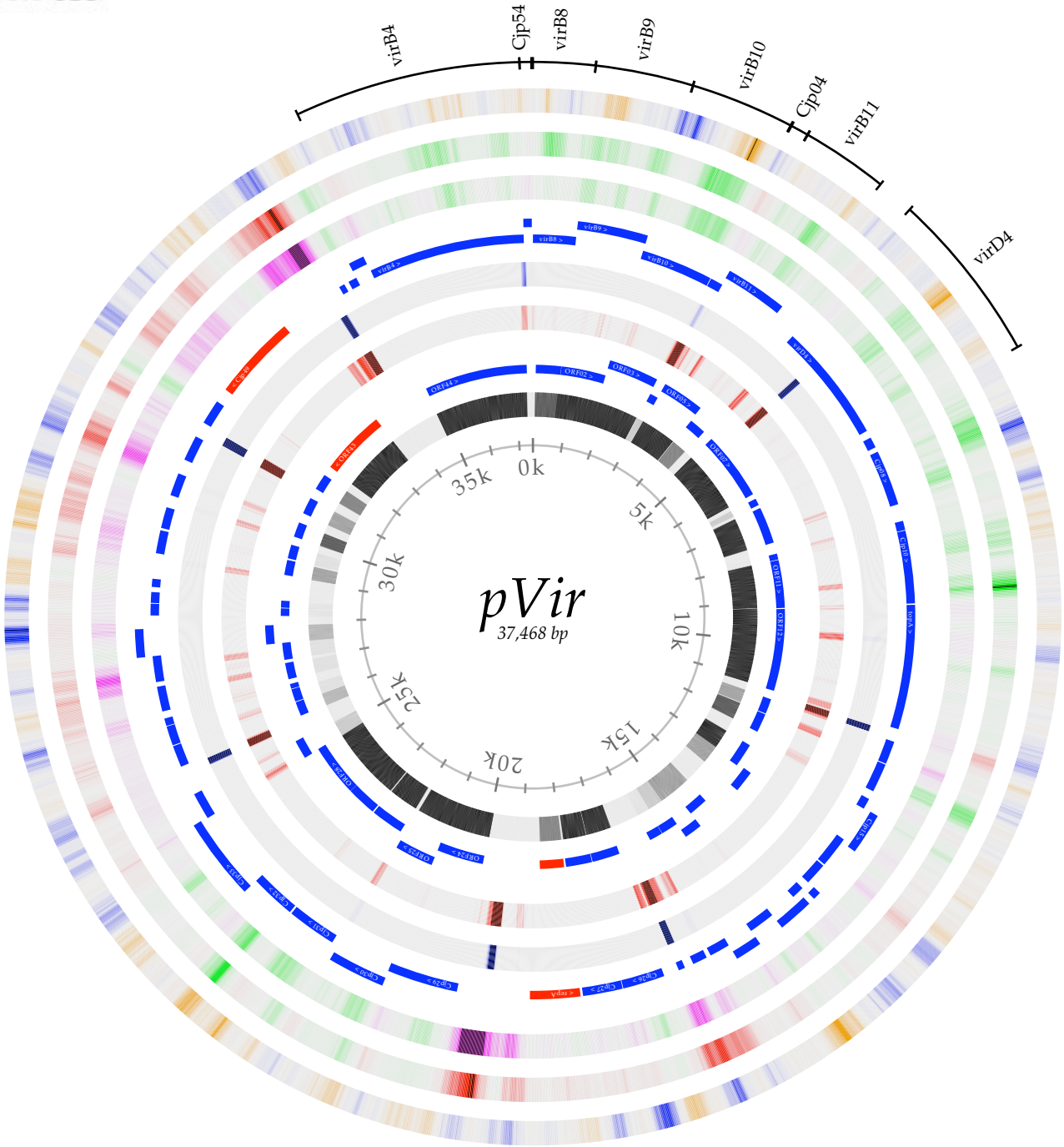


Fig. 10.5 Initiation of transcription in bacteria. In the first step, Sigma factor binds to the DNA on two locations (in the case of Sigma 70 the -35 and -10 sites). RNA polymerase (a complex of two α, one β and one β' subunit) binds next, after which the DNA wraps around the protein. Sigma induces local strand separation so that RNA polymerase starts producing RNA (*in green*). The Sigma factor is then released and RNA polymerase proceeds along the DNA, moving with a local bubble of melted DNA (*indicated by the arrows*)



Intrinsic Curvature
dev avg
0.18 0.34

Stacking Energy
dev avg
-7.55 -6.04

Position Preference
dev avg
0.14 0.22

Annotations:
CDS +
CDS -

Probability of Opening
dev avg
-0.34 0.38

Destabilisation energy
dev avg
1.88 14.98

Annotations:
eCDS +
eCDS -

EasyGene -logP
fix avg
0.00 10.00

Resolution: 15

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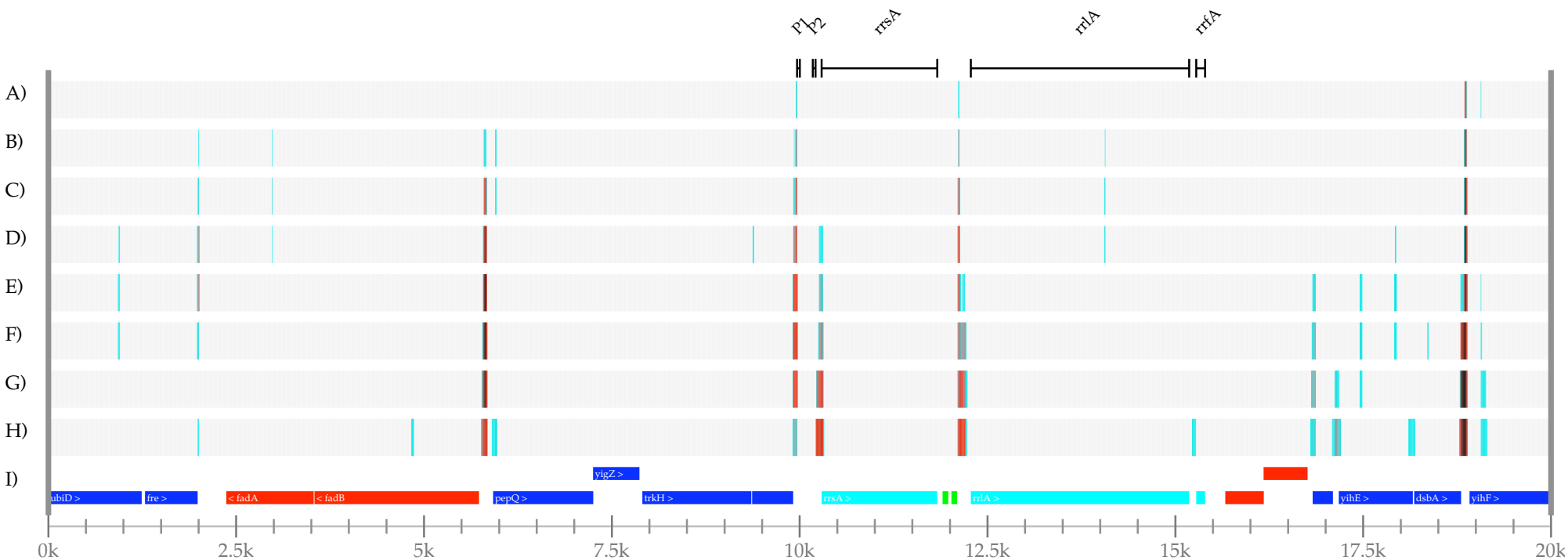
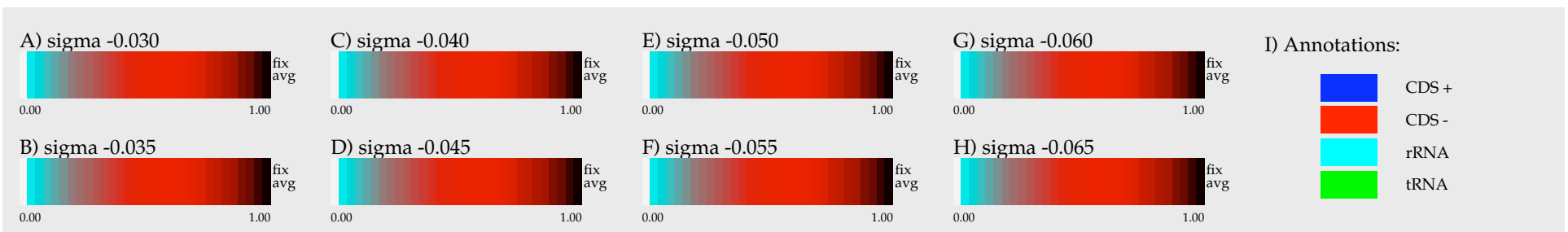
Ecoli_K12_MG1655 rrsA

20,000 bp



Resolution: 9



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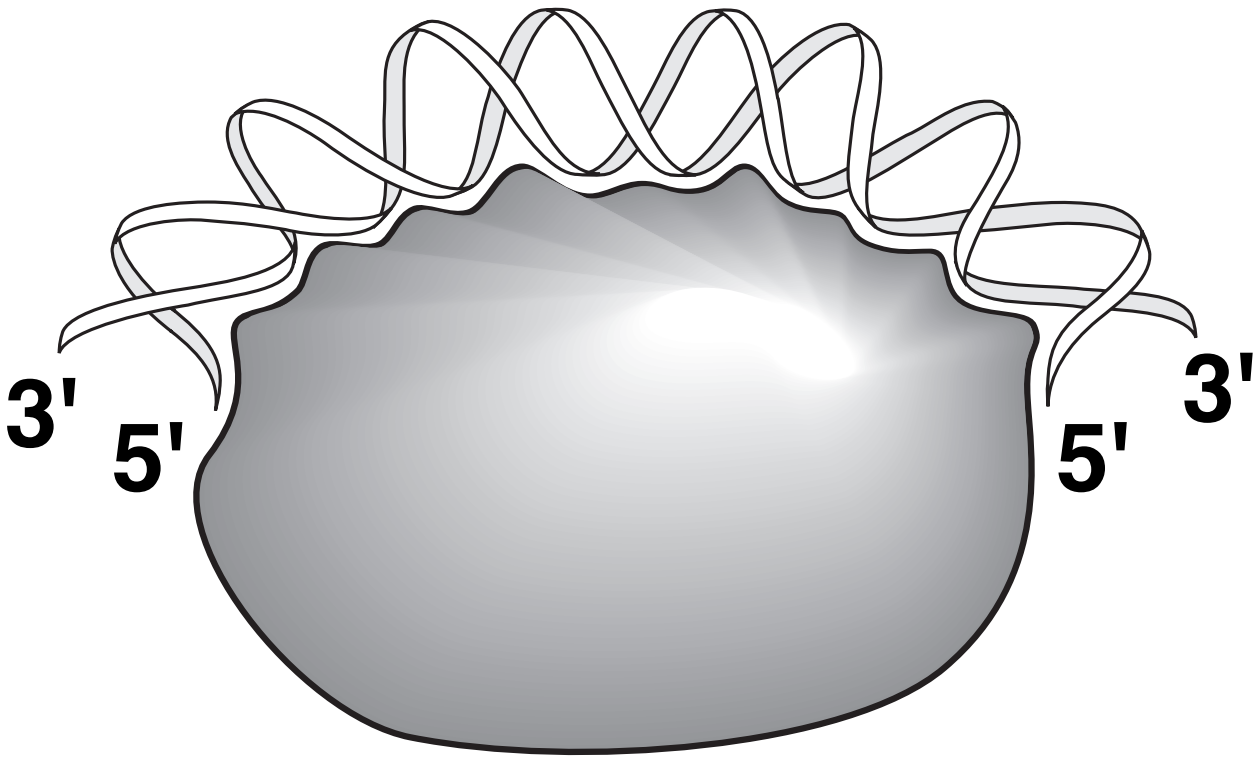
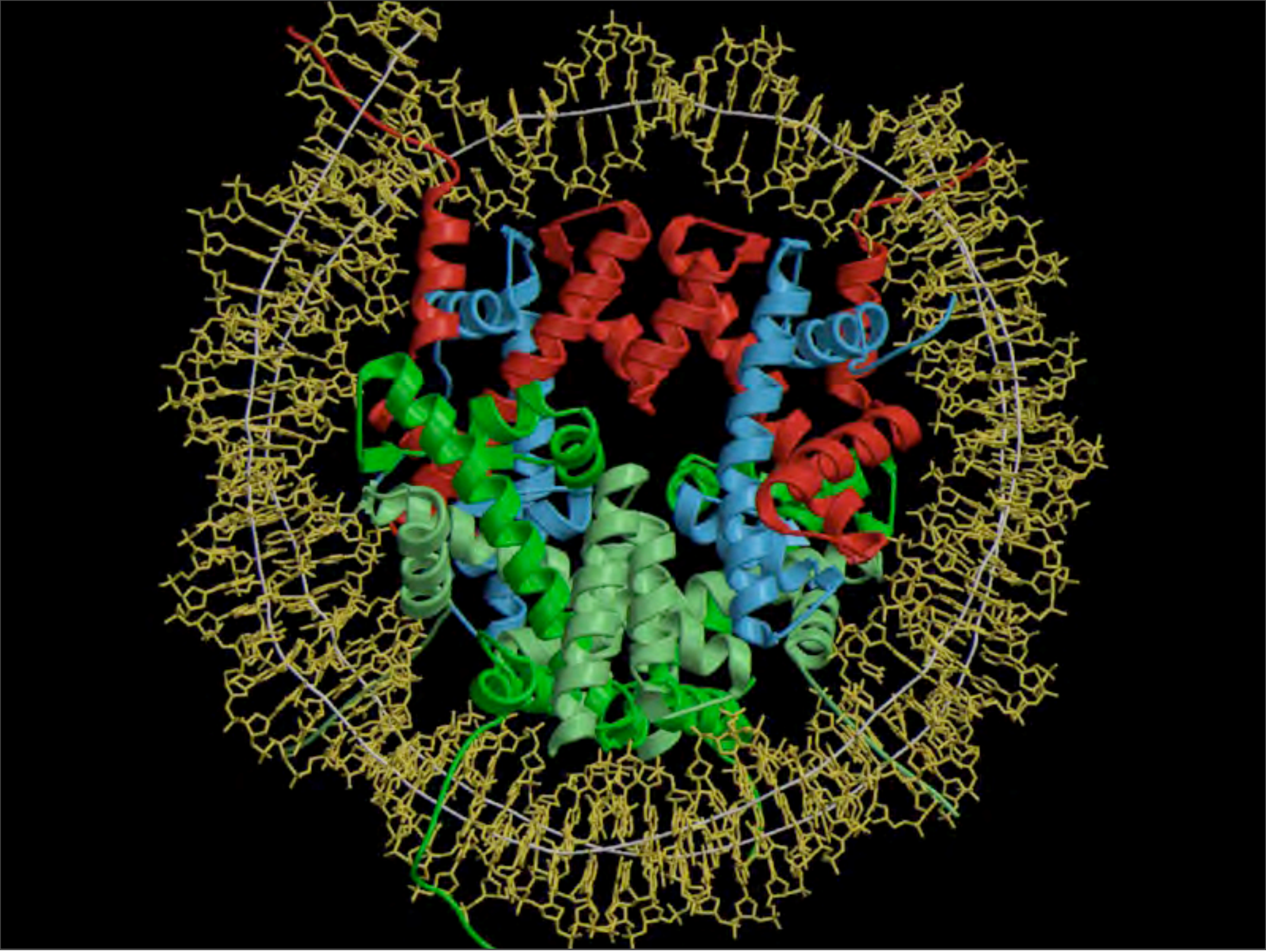
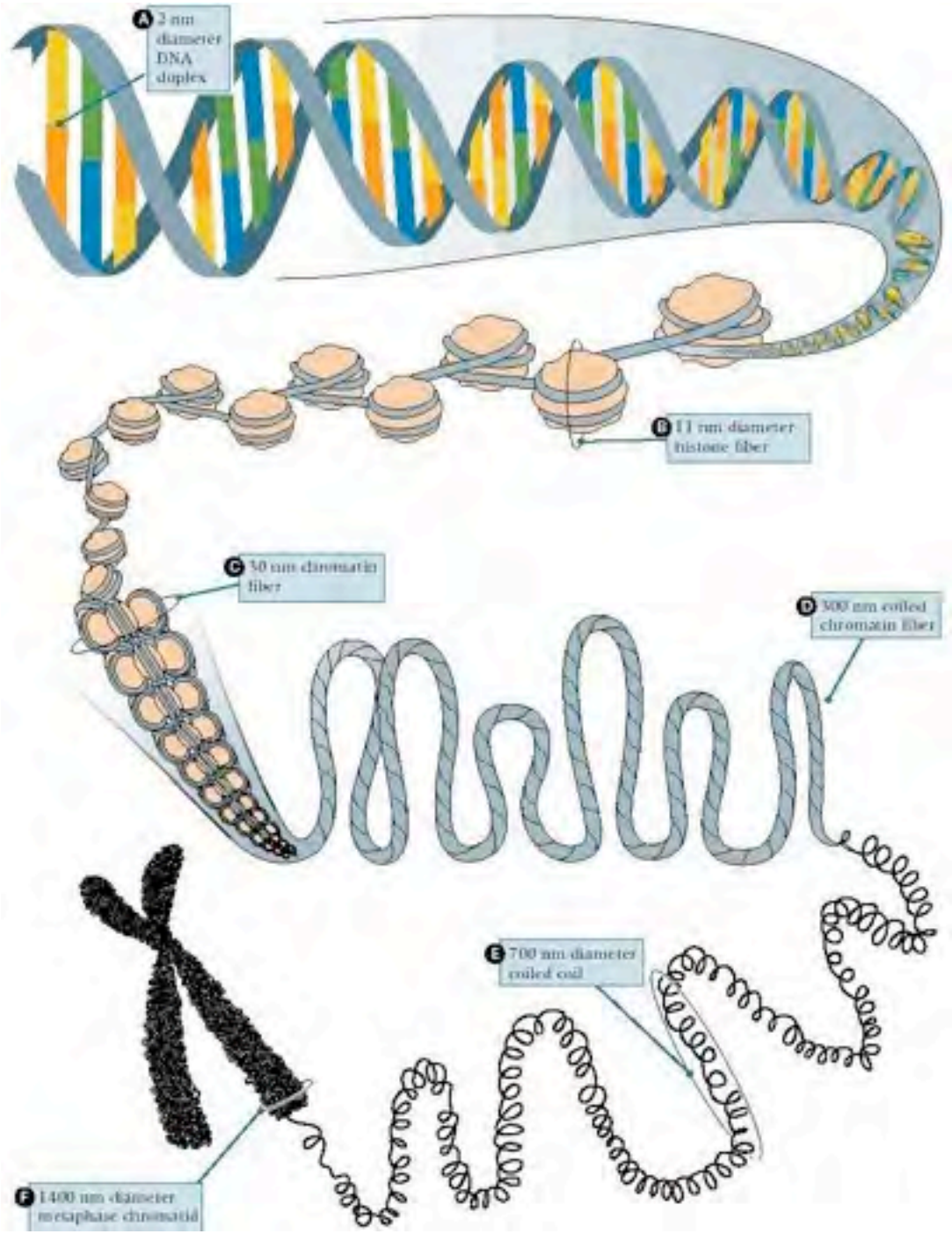
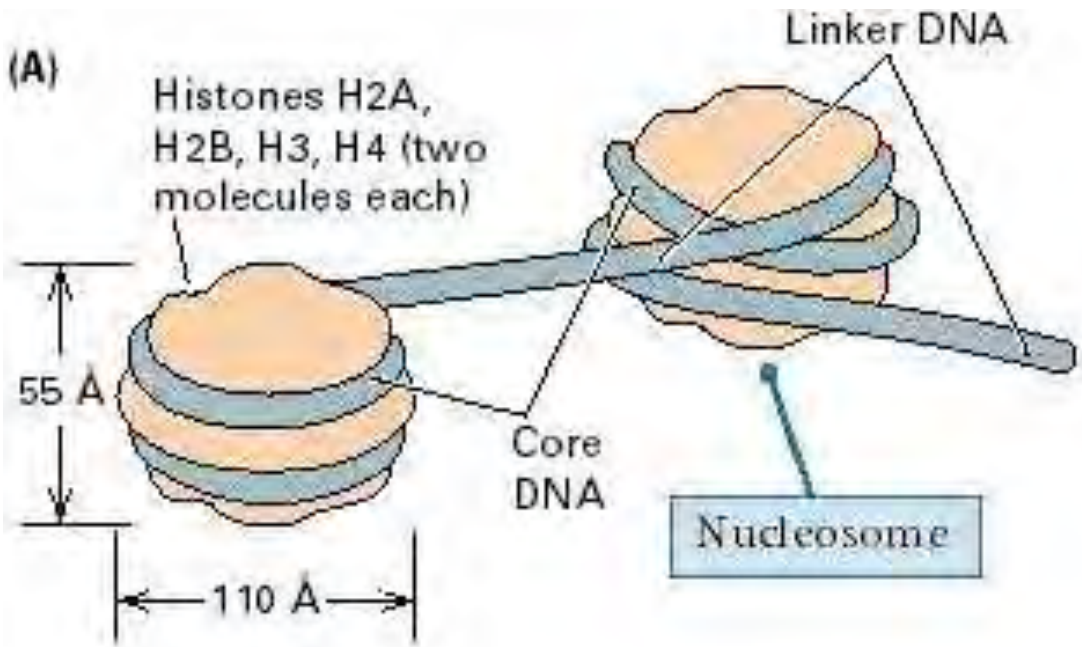
SIDD ATLAS

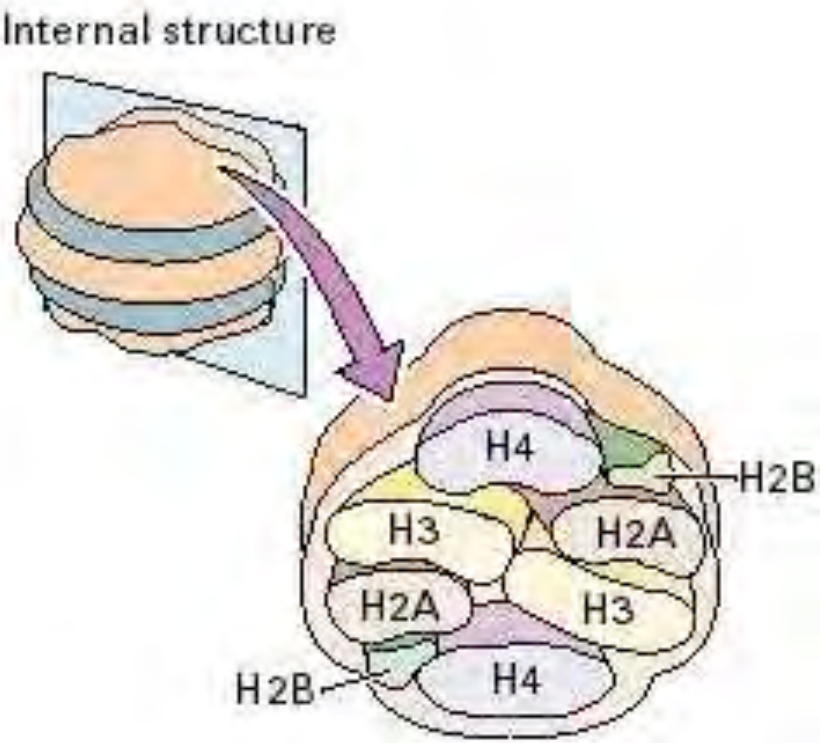
Pause

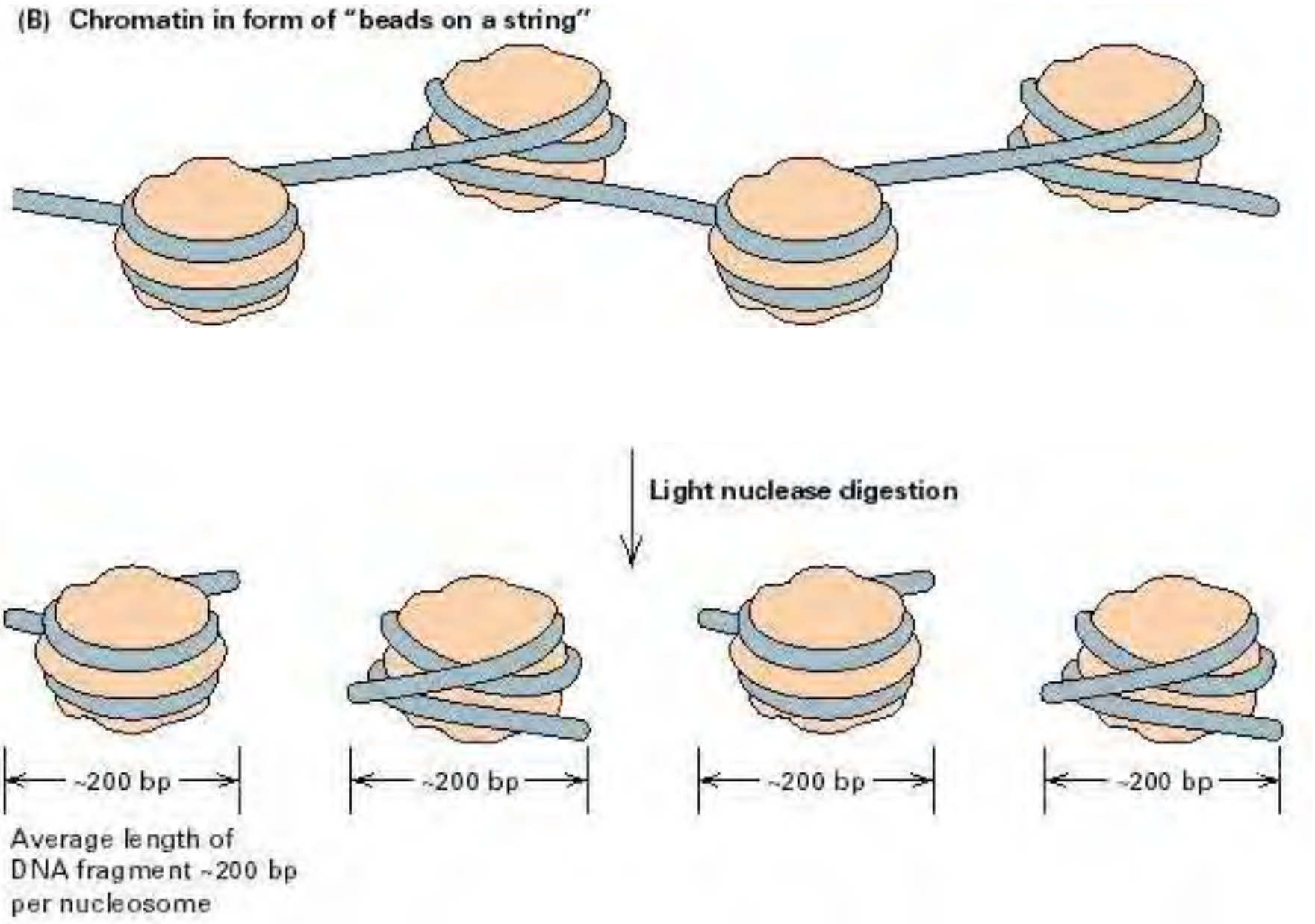

3'
5'
5'
3'

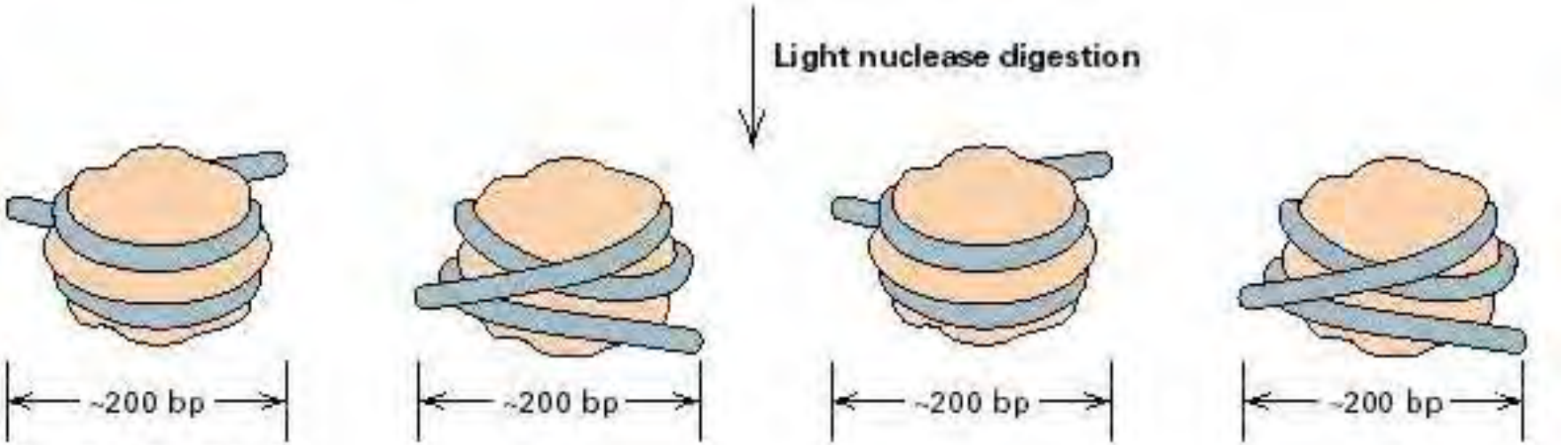



A 2 nm diameter DNA duplex
B 11 nm diameter histone fiber
C 30 nm chromatin fiber
D 300 nm coiled chromatin fiber
E 700 nm diameter coiled coil
F 1400 nm diameter metaphase chromatid

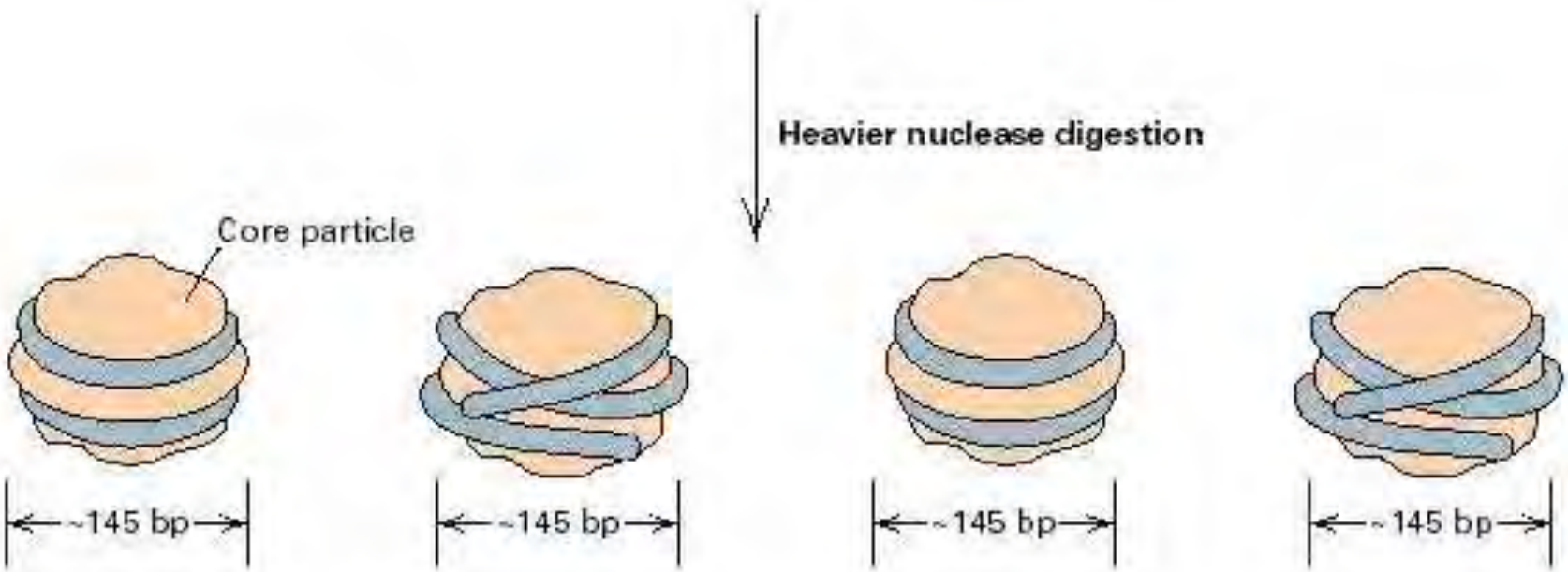

(A)
Histones H2A, H2B, H3, H4 (two molecules each)
Linker DNA
55 Å
110 Å
Core DNA
Nucleosome


Internal structure
H4
H2B
H3
H2A
H2A
H3
H2B
H4


(B) Chromatin in form of "beads on a string"
Light nuclease digestion
~200 bp
~200 bp
~200 bp
~200 bp
Average length of
DNA fragment ~200 bp
per nucleosome



Average length of DNA fragment ~200 bp per nucleosome



Average length of core DNA ~145 bp per core particle

"Travers" trinucleotide scale:

Satchwell,S.C., Drew,H.R., and Travers,A.A., "Sequence periodicities in chicken nucleosome core DNA", J. Mol. Biol., **191**:659-675, (1986).

NOTE: we use a (slight) modification, in which the absolute value (magnitude) of the values is used to reflect trinucleotides which tend to exclude nucleosomes.

Baldi,P., Brunak,S., Chauvin,Y., and Krogh,A., "Naturally occurring nucleosome positioning signals in human exons and introns",

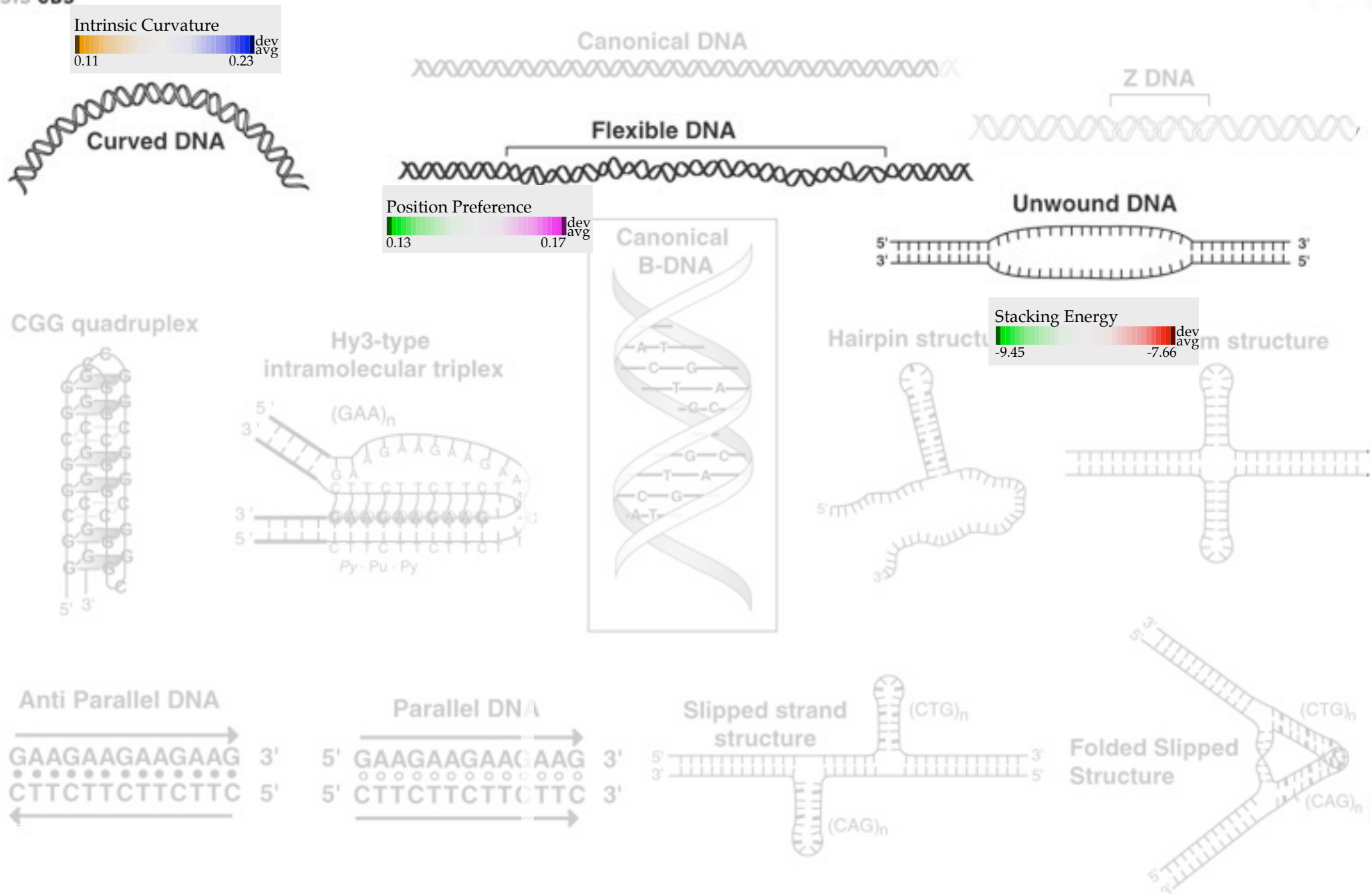
J. Mol. Biol., **263**:503-510, (1996).

trinuc.	% Out
AAT/ATT	-0.280
AAA/TTT	-0.274
CCA/TGG	-0.246
AAC/GTT	-0.205
ACT/AGT	-0.183
CCG/CGG	-0.136
ATC/GAT	-0.110
AAG/CTT	-0.081
CGC/GCG	-0.077
AGG/CCT	-0.057
GAA/TTC	-0.037
ACG/CGT	-0.033
ACC/GGT	-0.032
GAC/GTC	-0.013
CCC/GGG	-0.012
ACA/TGT	-0.006
CGA/TCG	-0.003
GGA/TCC	0.013
CAA/TTG	0.015
AGC/GCT	0.017
GTA/TAC	0.025
AGA/TCT	0.027
CTC/GAG	0.031
CAC/GTG	0.040
TAA/TTA	0.068
GCA/TGC	0.076
CTA/TAG	0.090
GCC/GGC	0.107
ATG/CAT	0.134
CAG/CTG	0.175
ATA/TAT	0.182
TCA/TGA	0.194

High position pref.

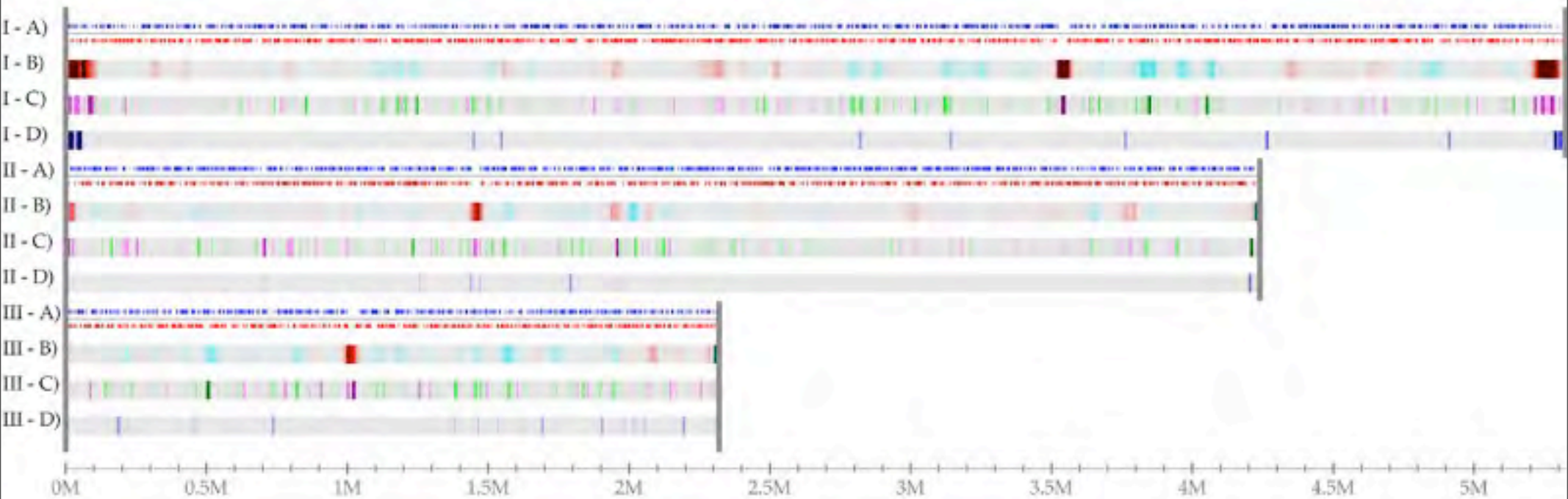
Low position pref.

High position pref.

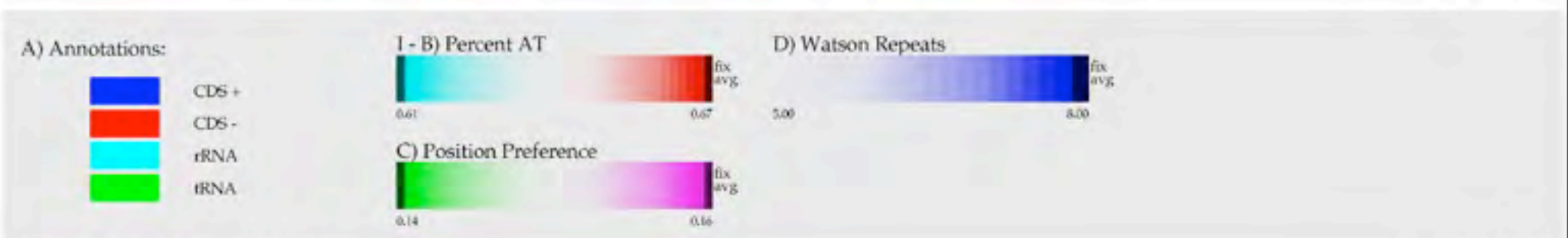

Intrinsic Curvature
dev
avg
0.11
0.23
Curved DNA
Canonical DNA
Z DNA
Flexible DNA
Position Preference
dev
avg
0.13
0.17
Unwound DNA
5'
3'
3'
5'
Canonical
B-DNA
Stacking Energy
dev
avg
-9.45
-7.66
CGG quadruplex
Hy3-type
intramolecular triplex
(GAA)n
Py · Pu · Py
Hairpin structu
m structure
Anti Parallel DNA
5' GAAGAAGAAGAAG 3'
3' CTTCTTCTTCTTC 5'
Parallel DNA
5' GAAGAAGAAGAAG 3'
5' CTTCTTCTTCTTC 3'
Slipped strand
structure
(CTG)n
(CAG)n
Folded Slipped
Structure
(CTG)n
(CAG)n

Schizosaccharomyces pombe

All Three Chromosomes *11,896,623 bp total*



Resolution: 1066



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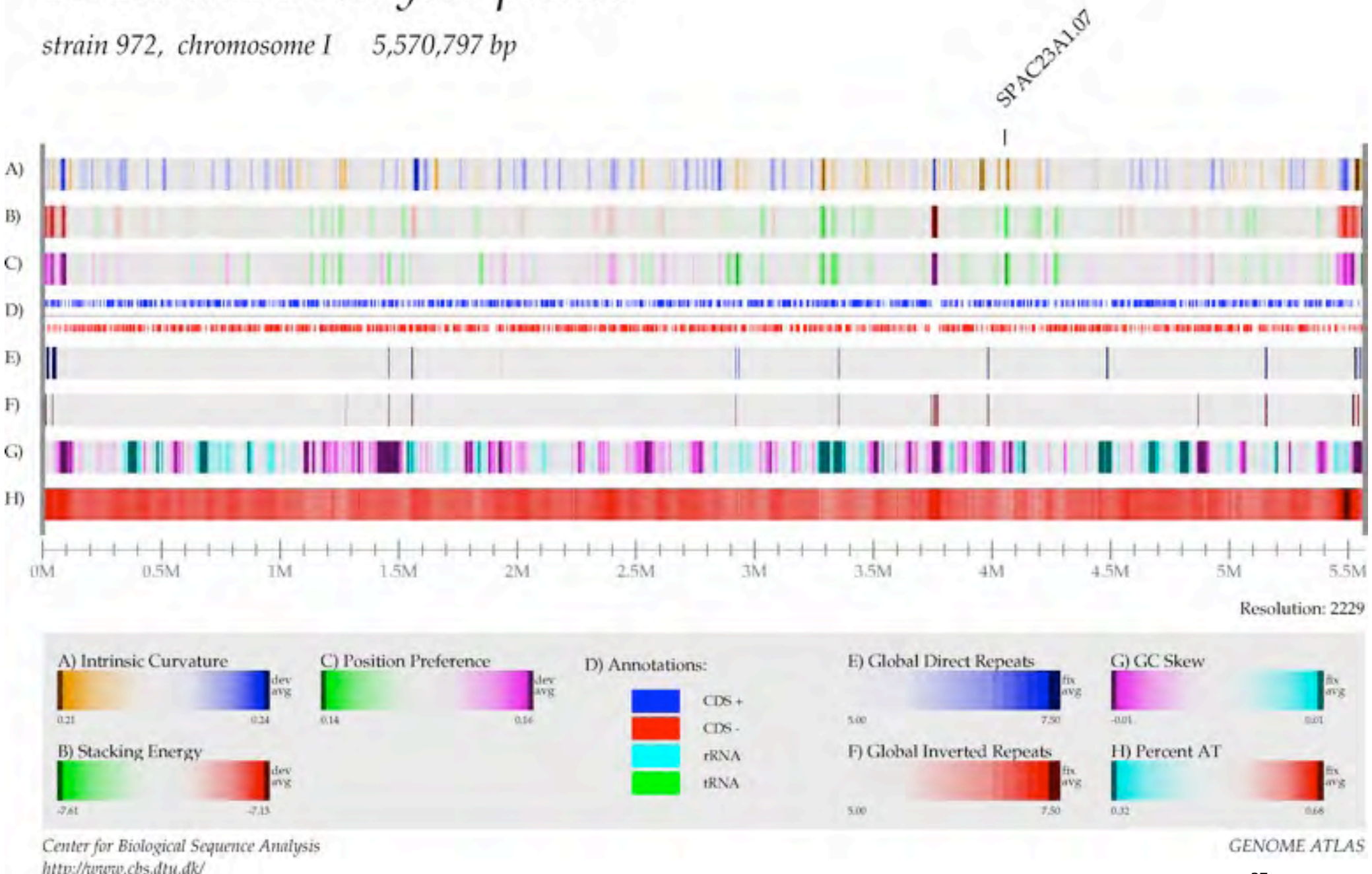
Nature, **415**:871-880, (2002).

Schizosaccharomyces pombe

strain 972, chromosome I 5,570,797 bp



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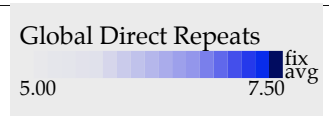
DNA Conformation and Transcription, chapter 14, (edited by Takashi Ohyama, 2004).

DNA Conformation and Transcription, chapter 14, (edited by Takashi Ohyama, 2004).

Direct repeats



5'-AGAGAGAGATCTAGACTAGAGAGAGAGAGATACCCTAGAGAGAGAGAGAGAAAG-3'
3'-TCTCTCTCTAGATCTGATCTCCCTCTCTCTATGGGATCTCTCTCTCTCTCTTTC-5'

Local direct simple repeats

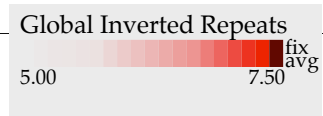
5'-AGGCAAAGTCGCCATGCTGCCATCTGGAGGCAAAGTCGCCATGCTGCCATCTGG-3'
3'-TCCGTTTCAGCGGTACGACGGTAGACGTCCGTTTCAGCGGTACGACGGTAGACC-5'

Local direct repeats

5'-AGGCAAAGTCGCCATGCTGCCATCTGGTGCCCAGGCAAAGTCGCCATGCTGCCATCTGG-3'
3'-TCCGTTTCAGCGGTACGACGGTAGACGACGGGTCCGTTTCAGCGGTACGACGGTAGACC-5'

Local direct repeats with spacer

Inverted repeats



5'-AGGCAAAGTCGCCATGCTGCCATCTGGCCAGATGGCAGCATGGCGACTTTGCCT-3'
3'-TCCGTTTCAGCGGTACGACGGTAGACCGGTCTACCGTCGTACCGCTGAAACGGA-5'

Local inverted repeat

5'-AGGCAAAGTCGCCATGCTGCCATCTGGTGCCCCCAGATGGCAGCATGGCGACTTTGCCT-3'
3'-TCCGTTTCAGCGGTACGACGGTAGACCACGCCGGTCTACCGTCGTACCGCTGAAACGGA-5'

Inverted repeat with spacer

5'-AGGCACGTGAGAATGAATTCCTGCTTTAGATCTAAAAGGCAAAGCTTTGCCT-3'
3'-TCCGTGCACTCTTACTTAAGGACGAAATCTAGATTTTCCGTTTCGAAACGGT-5'

Palindromic repeats

Mirror and Everted repeats

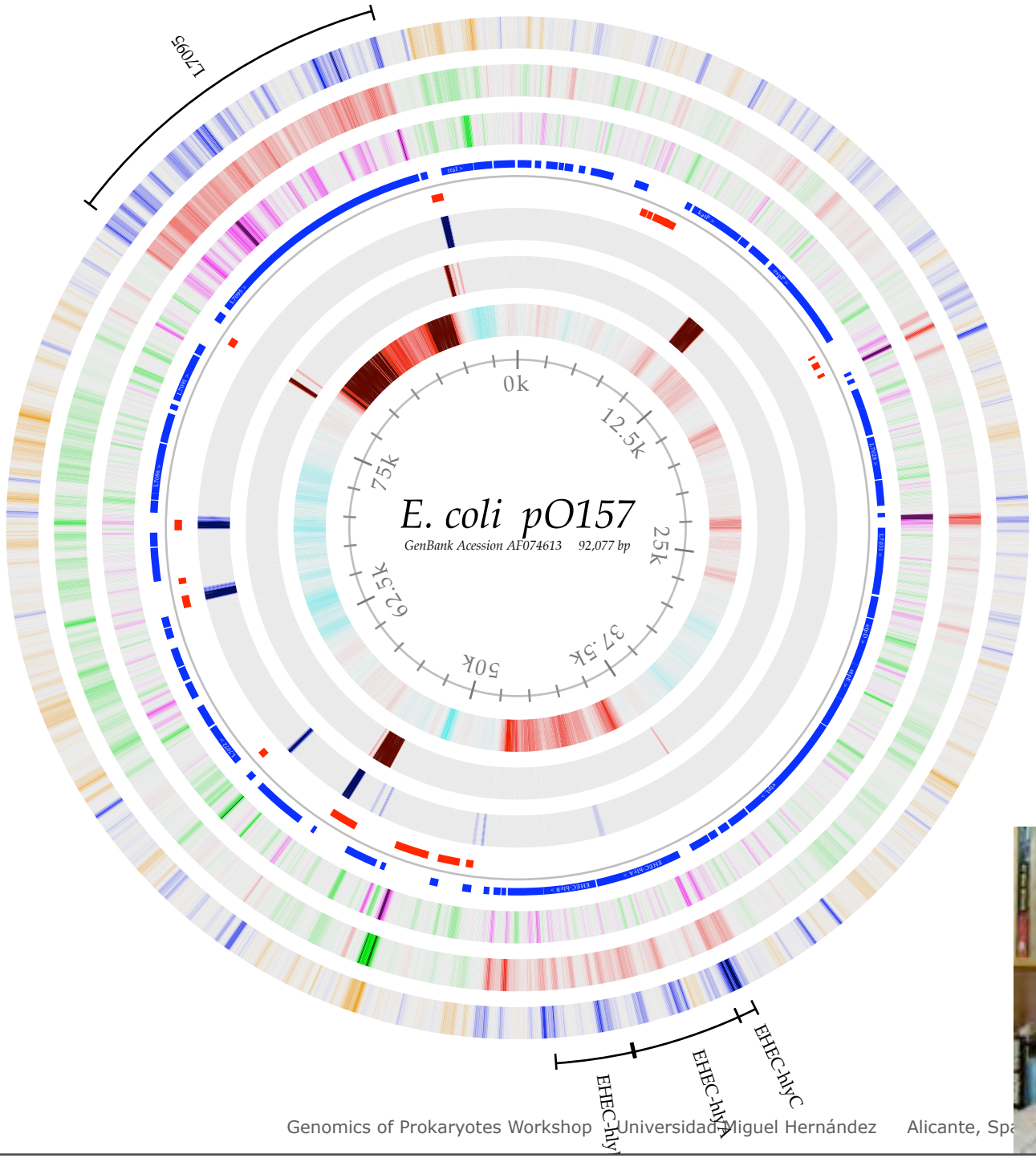
5'-AGGCAAAGTCGCCATGCTGCCATCTGGGGTCTACCGTCGTACCGCTGAAACGGA-3'
3'-TCCGTTTCAGCGGTACGACGGTAGACCCCAGATGGCAGCATGGCGACTTTGCCT-5'

Mirror repeat

5'-AGGCAAAGTCGCCATGCTGCCATCTGGTCCGTTTCAGCGGTACGACGGTAGACC-3'
3'-TCCGTTTCAGCGGTACGACGGTAGACCAGGCAAAGTCGCCATGCTGCCATCTGG-5'

Everted repeat

Introducing the "Genome Atlas"



Intrinsic Curvature

0.08 0.30

Stacking Energy

-9.52 -6.41

Position Preference

0.11 0.17

Annotations:

CDS +

CDS -

Watson Repeats

5.00 7.50

Crick Repeats

5.00 7.50

Percent AT

0.30 0.70

Resolution: 37

Friis, Jensen, and Ussery

Genetica, **108**:47-51, (2000).

http://www.cbs.dtu.dk/
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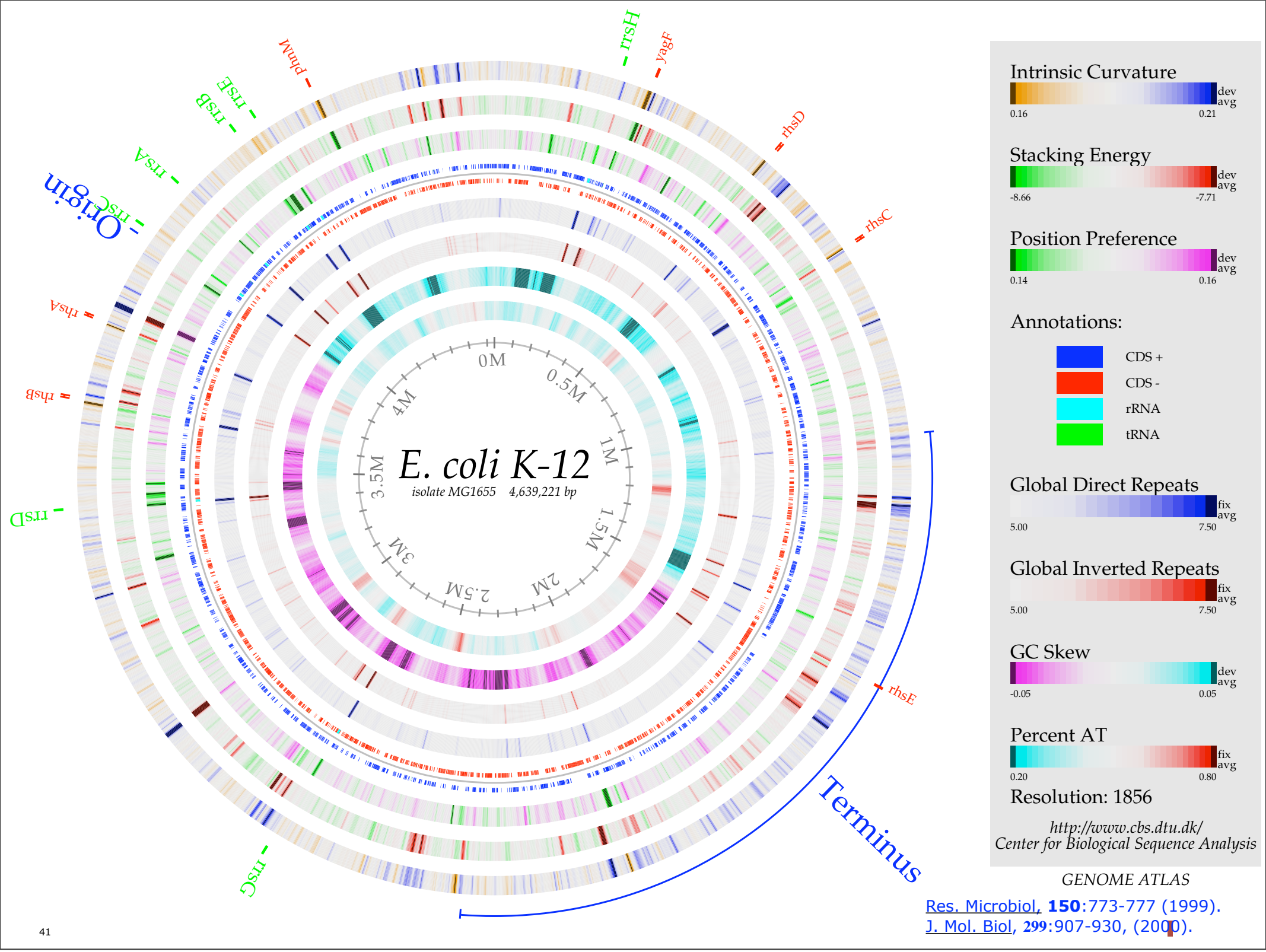
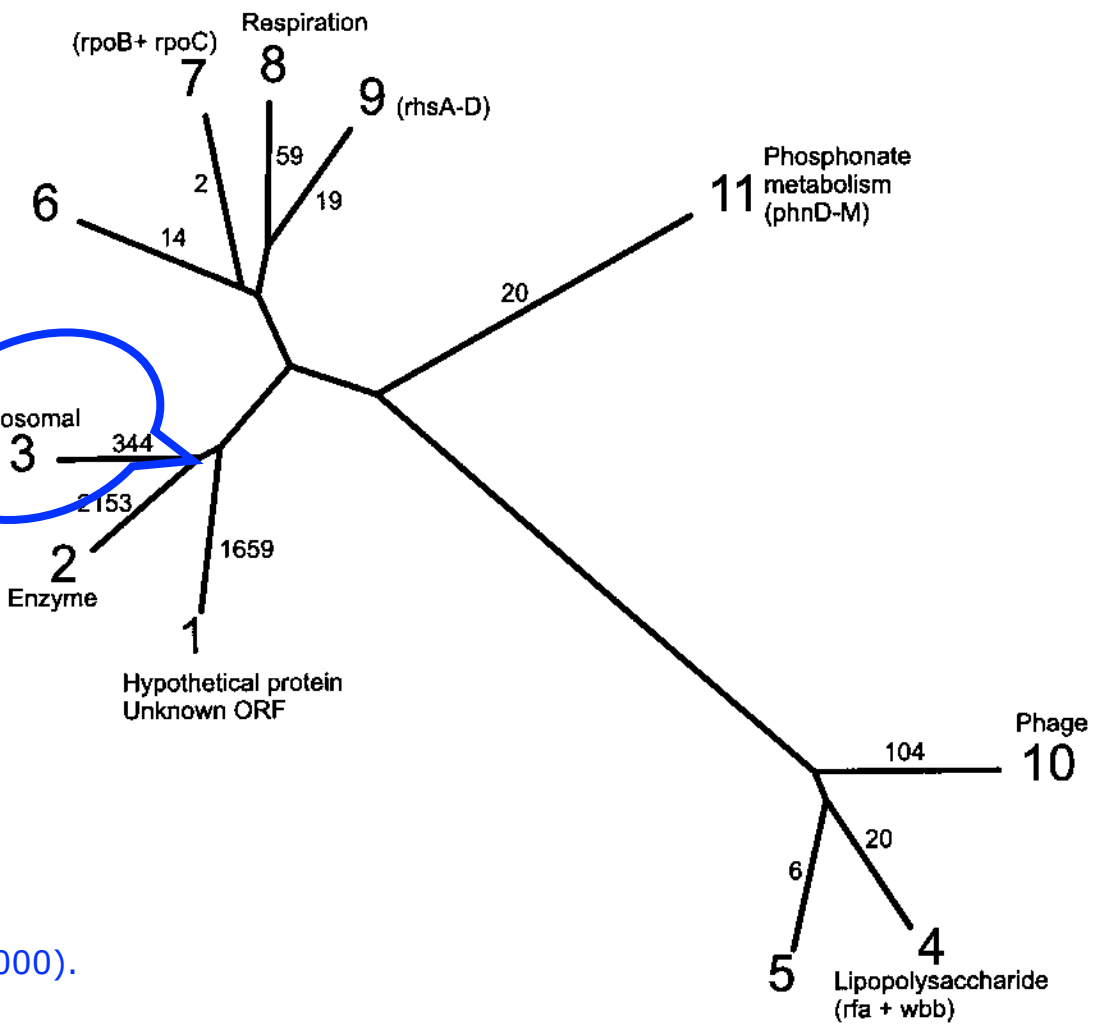
GENOME ATLAS



GENOME ATLAS

Res. Microbiol, **150**:773-777 (1999).
J. Mol. Biol, **299**:907-930, (2000).

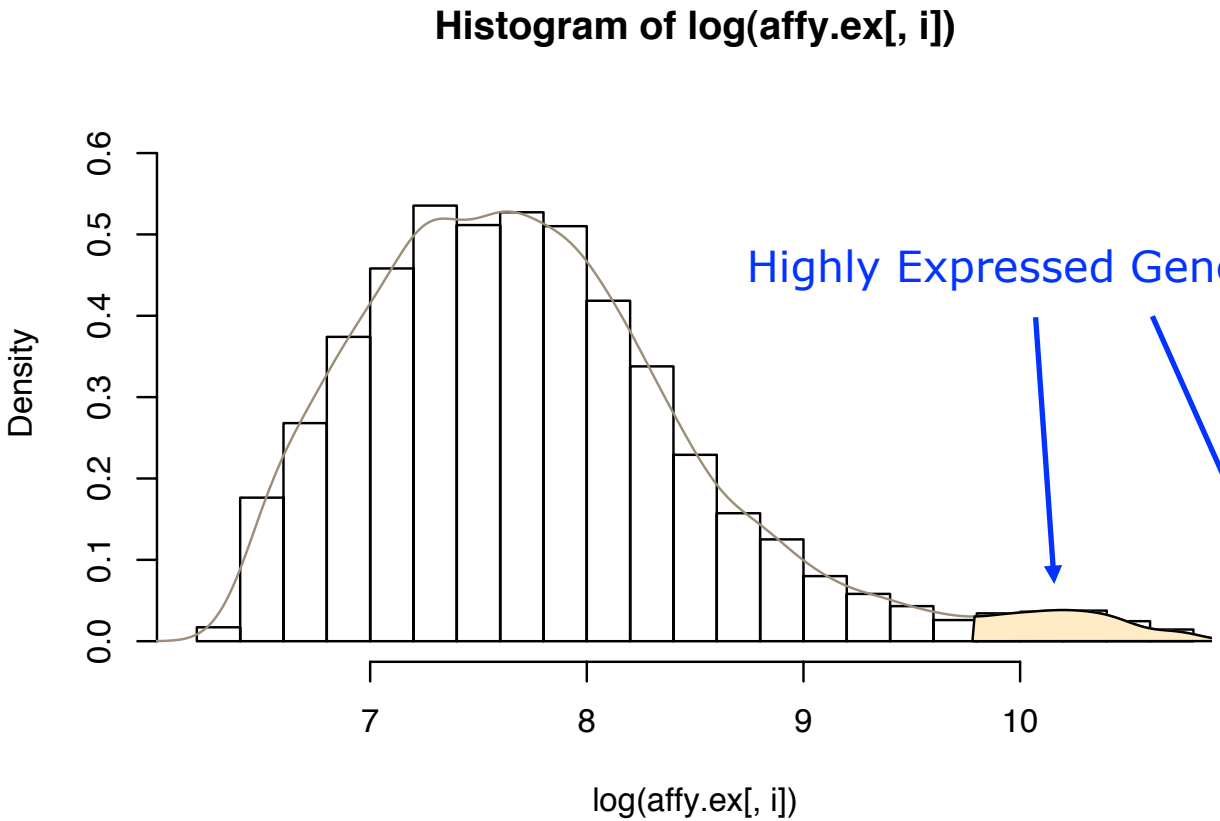
DNA Structural Atlas for Escherichia coli



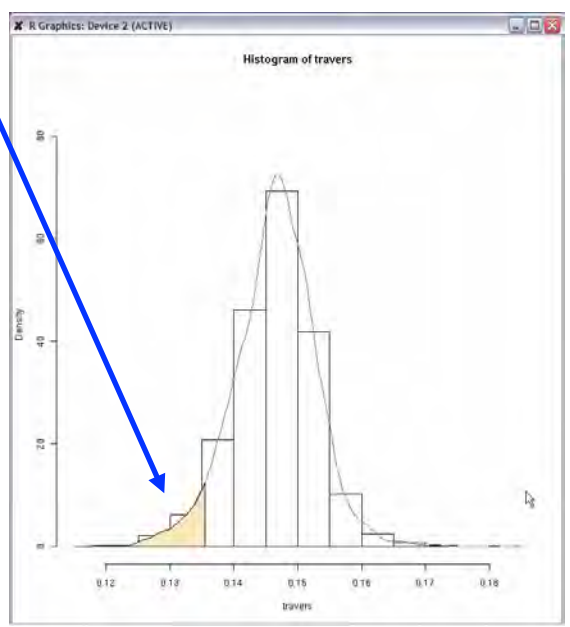
low position preference

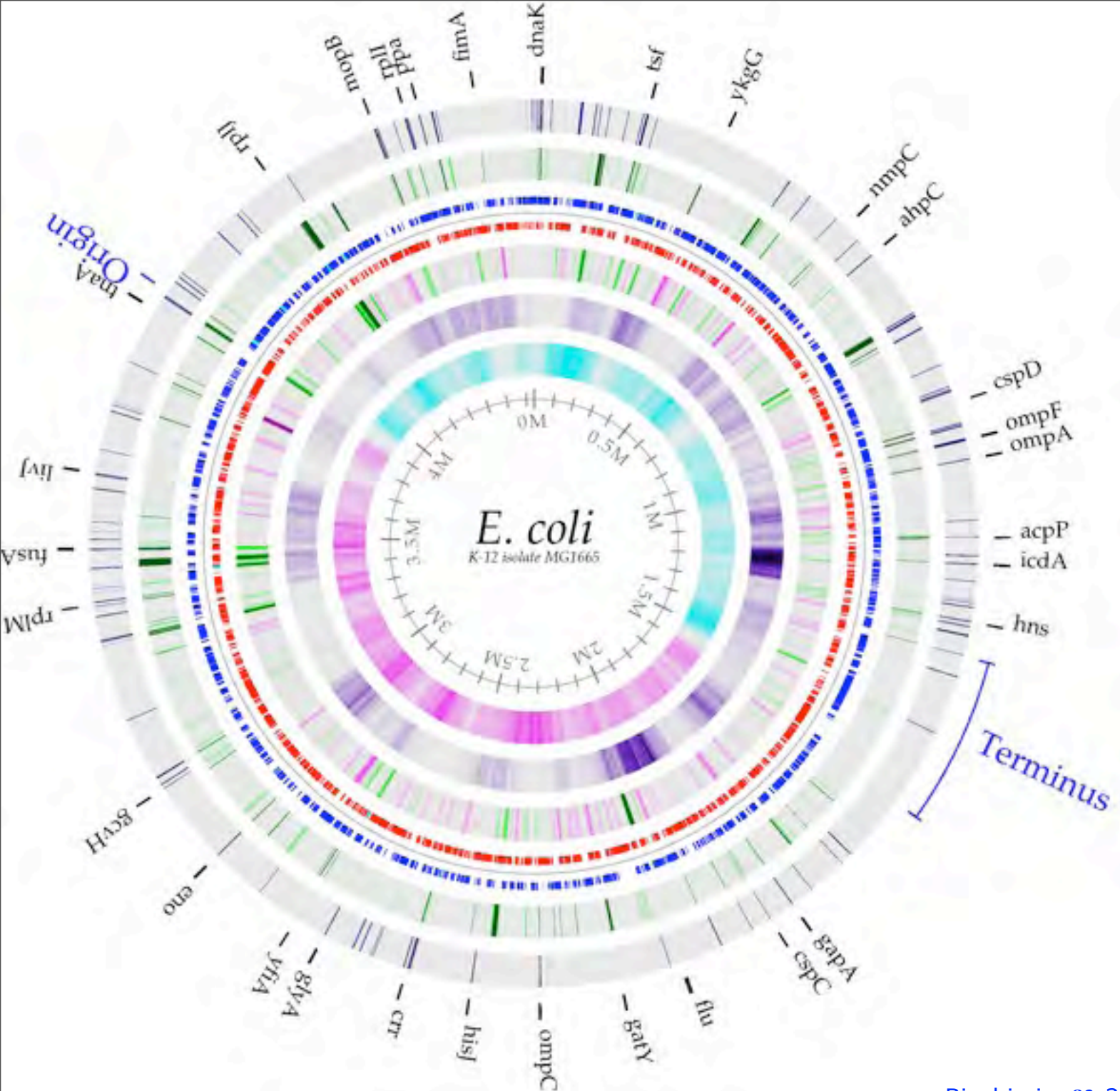
J. Mol. Biol, **299**:907-930, (2000).

Figure 7. Structural cluster analysis. Distance tree showing the relative location of 11 gene clusters based on average structural measures. The number of genes in



Highly Expressed Genes





Biochimie, 83:201-212, (2001).

Monday, 12 December, 2011