

TMS145: Introduction to (Mathematical Statistics and) **Bioinformatics**

Graham Kemp

<http://www.cse.chalmers.se/~kemp/teaching/TMS145/>

- **Structural Bioinformatics (3 lectures)**
Topics include: protein conformation, geometry calculations, secondary structure assignment, structural classification, stereochemical quality assessment, comparative modelling, fold recognition, secondary structure prediction.
- **Sequence Alignment (2 lectures)**
Topics include: pairwise global alignment, pairwise local alignment, dynamic programming, heuristic methods for finding local alignments, derivation and use of substitution matrices, multiple sequence alignment.

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Some challenges in structural bioinformatics

The protein folding problem

- given the sequence, what is the structure?

The docking problem

- given two structures, will they associate?
- what is the docking orientation?

Predicting function from structure

Designing new functionalities

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Introduction to Structural Bioinformatics

Lecture 1 — Aims

- To introduce the basic principles of protein conformation.

Lecture 1 — Objectives

After this lecture you will:

- be familiar with the basic features of protein conformation, and the abbreviations and symbols used in describing these;
- be aware of the twenty amino acid residues that are commonly found in proteins, and some of their properties;
- know about different levels of protein structure;
- understand how distances and angles can be calculated;
- be able to recognise common protein secondary structure elements and understand how these can be recognised automatically.

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Levels of protein structure

Primary structure

- amino acid sequence

Secondary structure

- assignment of helices and strands

Tertiary structure

- the 3D structure
- assembly and interaction of helices and sheets

Quaternary structure

- assembly of subunits

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Protein Data Bank entry (extract)

```
COMPND      TRIOSE PHOSPHATE ISOMERASE (E.C.5.3.1.1)
SOURCE      CHICKEN (GALLUS GALLUS) BREAST MUSCLE
AUTHOR      D.W.BANNER,A.C.BLOOMER,G.A.PETSKO,D.C.PHILLIPS,
AUTHOR      2 I.A.WILSON
:
JRNL        AUTH   D.W.BANNER,A.C.BLOOMER,G.A.PETSKO,D.C.PHILLIPS,
JRNL        AUTH 2 I.A.WILSON
JRNL        TITL   ATOMIC COORDINATES FOR TRIOSE PHOSPHATE ISOMERASE
JRNL        TITL 2 FROM CHICKEN MUSCLE
JRNL        REF    BIOCHEM.BIOPHYS.RES.COMM.      V. 72   146 1976
JRNL        REFN   ASTM BBRCA9 US ISSN 0006-291X      146
:
REMARK      2 RESOLUTION. 2.5 ANGSTROMS.
:
SEQRES      1 A   247  ALA PRO ARG LYS PHE PHE VAL GLY GLY ASN TRP LYS MET
SEQRES      2 A   247  ASN GLY LYS ARG LYS SER LEU GLY GLU LEU ILE HIS THR
:
ATOM        1 N   ALA A   1      43.240  11.990  -6.915  1.00  0.00
ATOM        2 CA  ALA A   1      43.888  10.862  -6.231  1.00  0.00
ATOM        3 C   ALA A   1      44.791  11.378  -5.094  1.00  0.00
ATOM        4 O   ALA A   1      44.633  10.992  -3.937  1.00  0.00
ATOM        5 CB  ALA A   1      44.722  10.051  -7.240  1.00  0.00
ATOM        6 N   PRO A   2      45.714  12.244  -5.497  1.00  0.00
ATOM        7 CA  PRO A   2      46.689  12.815  -4.561  1.00  0.00
ATOM        8 C   PRO A   2      46.042  13.601  -3.411  1.00  0.00
ATOM        9 O   PRO A   2      46.030  13.141  -2.267  1.00  0.00
:
```

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DSSP summary codes

H 4-helix (α -helix)
B residue in isolated β -bridge
E extended strand, participates in β -ladder
G 3-helix
I 5-helix
T H-bonded turn
S bend

Crambin (1CRN)

```
TTCCPSIVARSNFNVCRLLPGTPEAICATYTGCIIPGATCPGDYAN
EE SSSHHHHHHHHHHHHHTT HHHHHHHHS EE SSS TTS
```

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DSSP bridges

Antiparallel bridge:

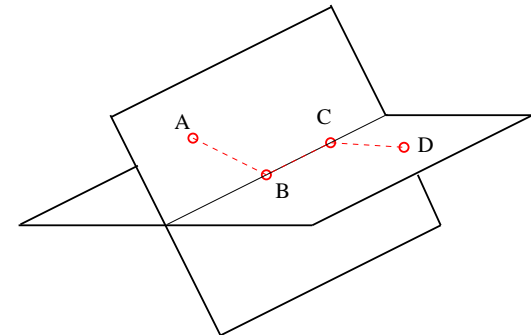
[hbond(i,j) and hbond(j,i)]
or
[hbond(i-1,j+1) and hbond(j-1,i+1)]

Parallel bridge:

[hbond(i-1,j) and hbond(j,i+1)]
or
[hbond(j-1,i) and hbond(i,j+1)]

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Dihedral angle



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