第三單元 蛋白質結構與穩定 Protein structure and stability

3.1 蛋白質各級結構定義/胜肽鍵的特徵 Protein structure hierarchy, peptide bond and Ramachandran plot
3.2 二級結構 - 螺旋 Secondary structure - alpha helix
3.3 二級結構 - 摺板與其他 Secondary structure - beta sheet and others
3.4 三、四級結構與纖維蛋白舉例 Tertiary and quaternary structure, Fibrous protein examples
3.5 蛋白質構型與維持構型之作用力 Protein conformation and maintaining forces
3.6 蛋白質折疊過程之探討 Protein folding

學習目標：

1. 瞭解蛋白質各級結構的定義，及維持各級結構的作用力。
2. 瞭解胜肽鍵的特性及限制。
3. 瞭解二級結構中螺旋(α-helix)及摺板(β-sheet)的結構特徵及相似、相異處。
4. 瞭解蛋白質折疊與變性的可能過程。

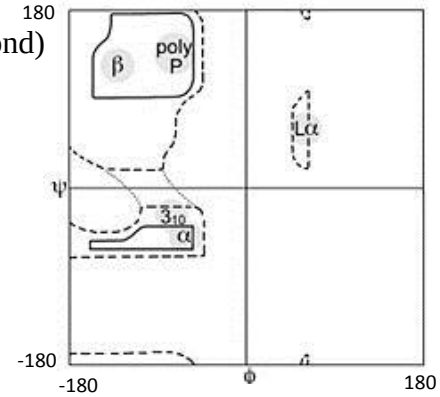
天堂筆記：

1. Protein structural hierarchy:
   - Primary structure 一級結構: amino acid sequence 序列 (covalent structure)
     - 胜肽鏈的胺基酸序列
   - Secondary structure 二級結構: recurring structural pattern
     - 胜肽鏈主幹所形成的重複或規律性結構
   - Tertiary structure 三級結構: 3D folding in space
     - 胜肽鏈栽在空間中的結構
   - Quaternary structure 四級結構: Subunits arrangement within a protein
     - 蛋白質由兩個以上次單元所組成時，這些次單元在空間中的組成或排列之結構

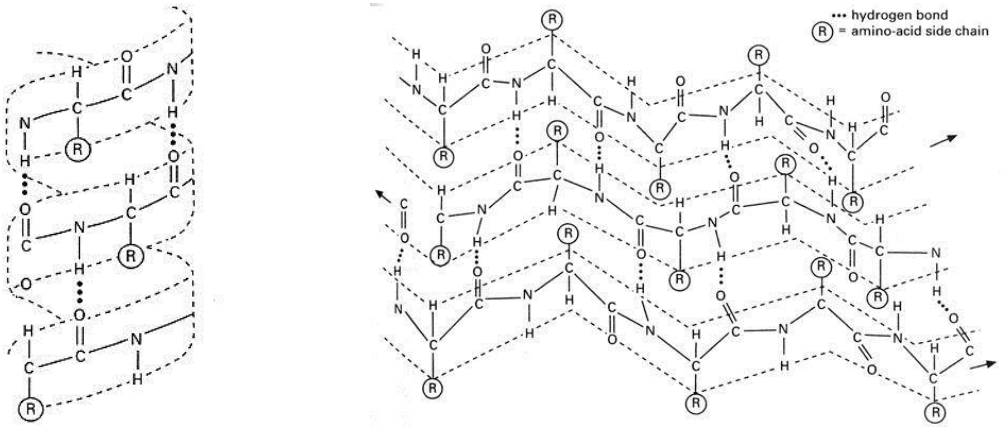
2. Polypeptide chain:
   - Backbone 主幹: -(N-Cα-C)$_i$-(N-Cα-C)$_{i+1}$-(N-Cα-C)$_{i+2}$-….
   - Side chain 支鏈: R group

3. Peptide bond
   - Peptide bond can't rotate (planar and rigid)
     - Electrons resonance (電子共振) between the carbonyl O and the amide N
     - Restricted rotation (torsion) angles: phi-ϕ (-Cα-C-) and psi-ψ (-N-Cα-)
     - Ramachandran plot

4. Secondary structure (local conformation, maintained by H-bond)
   - α-helix (α-螺旋)
     - Compact
     - Right-handed 右旋, 3.6 a.a./turn, 5.4 Å/turn
     - R-group extended outward
     - H-bond between backbone residues
       - ✓ -CO of residue $_i$ and the –NH of residue $_{i+4}$
       - ✓ Pro: helix breaker (ends α helix)



Ramachandran Plot



左: α-螺旋；右: β-摺板(反平行)。圖片來源: https://sallyarjoon.wordpress.com/tag/protein/

- β-conformation (β-sheet， β-摺板)
  - Extended, zigzag
  - H-bond between backbone residues
    - ✓ -CO of residue and the –NH of residue
  - Parallel (平行) and antiparallel (反平行) β-sheet
- β-turn
  - A 180 ° turn involves 4 a.a.
  - Favor Gly and Pro

5. Forces maintaining the protein structure
   - Strong interaction (covalent bonding): disulfide bond
   - Weak interaction (non-covalent bonding)
     - H-bond 氫鍵
     - Hydrophobic interaction 疏水性作用力
     - Ionic interaction 離子間作用力
     - Van der Waals interaction 凡得瓦力

6. Protein structure determination:
   - Primary structure determination:
     - Edman degradation;
     - Mass spectroscopy
     - Derived from DNA sequence
   - Secondary structure determination
     - Circular dichroism (CD, 圓二色極化光譜儀)
       - ✓ Estimate 2o structure content in a protein.
   - Tertiary and quaternary structure determination
     - X-ray crystallography
       - ✓ Protein crystal (蛋白質結晶) + X-ray diffraction (X-光繞射)
     - Nuclear Magnetic Resonance (NMR，核磁共振)

7. Fibrous proteins: long strands or sheets, usually function in support or protection
   - e.g. α-keratin 角質素, collagen 膠原蛋白

8. Globular proteins: compact shape, usually function in regulation
   - e.g. myoglobin 肌紅素, hemoglobin 血紅素

9. Protein conformation 構形:
   - Native: folded, active or functional state
     - Thermodynamically (熱力學) stable; lowest Gibbs free energy (G, 自由能)
   - Denatured 變性: unfolded state, inactive form, not functional

10. Protein folding 蛋白質摺疊
    - A cooperative (協同作用，互相合作) process
    - Process: local 2° structure first; then long-range interactions between structural elements to form 3° and 4° structures.
    - For soluble proteins : usually hydrophobic inside, hydrophilic outside
    - Assisted folding: chaperones, chaperonins (heat shock protein)
    - Misfolded protein and disease:
      - The prion disease (mad cow disease 狂牛症) and prion protein (PrP^C, PrP^{SC})
      - Alzheimer's disease 阿茲海默症, Parkinson's disease 巴金森斯症
        - ✓ β-amyloid 類澱粉蛋白

魔咒關鍵詞：

Protein structure (backbone vs side chain)
- Primary structure
- Secondary structure: α helix and β sheet
- Tertiary structure
- Quaternary structure

Peptide bond, rotation angle, Ramachandran diagram (plot)
- α-helix; β-conformation (β-sheet)

Globular (compact, soluble) protein: hydrophobic inside, hydrophilic outside
Fibrous protein (extended, insoluble)
Conformation : native vs denatured (active vs inactive, folded vs unfolded)
Weak (non-covalent) interaction vs Strong (covalent) interaction

H-bond	Peptide bond
Ionic interactions	Disulfide bond
Hydrophobic interactions	
Van der Waal interactions	

魔法參考書目:

1. 台大莊榮輝教授教學網頁: http://juang.bst.ntu.edu.tw/BCbasics/index.htm
2. Lehninger Principles of Biochemistry (2013), 6th ed, David L. Nelson, and Michael M. Cox, Freeman and Company, New York.
3. Principles of Biochemistry (2013) 4th ed. Voet, Voet, and Pratt. Wiley.
4. Biochemistry, a short course. (2015) John L. Tymoczko, Jeremy M. Berg, Lubert Stryer (3rd ed) W.H. Freeman & Company.

魔法練習題:

1. 請描述蛋白質各級結構之定義。
2. 為什麼胜肽鍵不可以旋轉?
3. 請描述蛋白質二級結構中α-螺旋與β-摺板的特徵。
4. 維持蛋白質結構的弱作用力有哪些?
5. 蛋白質「變性」(denature)是甚麼意思?