UNIVERSITY MEDICINE • EXERCISE SHEET

2.1 Proteins and protein structure

Name: _____ Class: _____ Date: _____ **Total: 23 marks**

KEY WORDS haemoglobin

Objective

Relate protein structure levels to function and compute oxygen capacity from first principles.

1 Key knowledge and worked examples

■ **The four levels**

Primary sequence → secondary helix/sheet → tertiary fold → quaternary assembly. Haemoglobin: $\alpha_2\beta_2$, 64.5 kDa, 4 O_2; sigmoid binding from cooperativity (Hill $n_H \approx 2.8$).

■ **Worked example: capacity from scratch**

15 g Hb/dL ÷ 64 500 g/mol × 4 sites ≈ 930 µmol O_2/dL ≈ 20.8 mL/dL ✓.

2 Practice

2.1 Order the four structure levels and name the bonds/forces dominant at each. [3]

2.2 Why does myoglobin bind O_2 hyperbolically but haemoglobin sigmoidally? [3]

2.3 A mutation swaps a surface glutamate for aspartate. Predict the structural impact and justify. [3]

3 Exam-style questions

3.1 Hb has 4 O_2 sites; p50 in tissues shifts with 2,3-BPG.

Explain the T↔R transition and why binding is cooperative. Compute the O_2 content of blood (15 g/dL Hb) in mL/dL. State what happens to that number in anaemia (Hb 7.5 g/dL) and the compensatory mechanism. [7]

3.2 (Fictional) HbS: Glu6Val on the β chain.

Explain how a single primary-structure change produces sickling at the quaternary level. State the trigger state (oxy/deoxy) and why. Predict the effect on oxygen capacity per molecule and on blood viscosity. [7]

Solutions

2.1

- Primary: peptide bonds; secondary: backbone H-bonds; tertiary: hydrophobic effect + H-bonds + disulfides; quaternary: same forces between subunits.

2.2

- Myoglobin is single-site (no partners to influence); haemoglobin's four sites communicate via T↔R subunit shifts – binding helps binding.

2.3

- Conservative surface swap (both negative, similar size): minimal impact – outside the core and the active site.

3.1

- T is low-affinity, R high; each O_2 binding shifts equilibrium toward R, so later sites bind more easily (sigmoid, $n_H \approx 2.8$).
- $15/64\,500 \times 4 \times 22\,400 \approx 20.8$ mL/dL ✓.
- Anaemia halves it to ~10.4 mL/dL; compensation is raised cardiac output and erythropoietin-driven red-cell production.

3.2

- Val6 creates a hydrophobic patch on the β surface; in the deoxy T state it docks into a pocket on another Hb, polymerising fibres.
- Trigger: deoxy (T-state conformation exposes the patch).
- Capacity per molecule unchanged (haem intact); viscosity rises and cells deform/occlude.