

University of Canterbury

# Mid Year Examination and Test Period 2007

Prescription Number(s):	BCHM 301
Paper Title:	Biochemistry 3

Time Allowed: 2.5 HOURS

Number of pages: SIX

Answer **THREE** questions out of four.

All questions are of equal value.

**TURN OVER**



1. Suppose you have been employed as a protein biochemist to work on a contract funded by the meat industry. Funding is available to discover ways to improve the commercial value of inedible muscle tissue and, because of your expert knowledge of the proteins of muscle, you have been asked to advise on the merits of two project ideas, (a) and (b) below.

**For each project idea, comment on the likely feasibility of the proposal. Include in your answer a detailed account of the predicted impact of the proposed treatment on the structure and function of the proteins of muscle. In each case, describe the techniques you would use to find out whether your predictions are correct.**

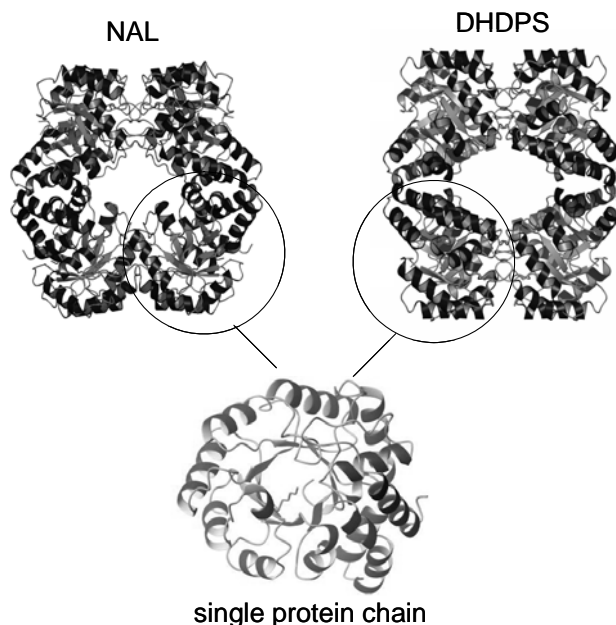
- (a) (10 marks)

One of the reasons that meat becomes tough is that the animal undergoes rigor mortis after slaughter. Rigor mortis sets in when the ATP supply to the muscle is depleted. It is proposed to treat the muscle with a cheap, readily available ATP analogue in order to prevent the onset of rigor mortis and make previously inedible cuts of meat more palatable. The meat industry funding panel would like you to comment on whether this is feasible.

- (b) (10 marks)

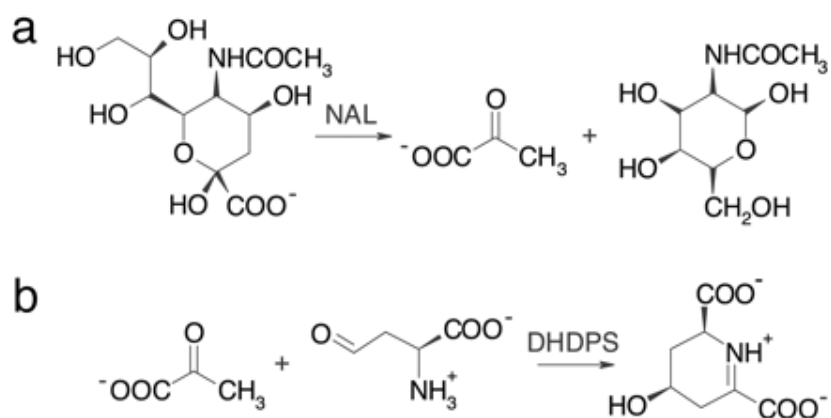
The waste muscle proteins represent a potential source material for assembly of novel biomaterials. It is proposed to digest the inedible muscle tissue with proteases and use the resulting soluble proteins to manufacture tough fibrous materials. Two types of target biomaterial have been identified: (i) based on the native structure of the protein and (ii) based on the amyloid fibril. The meat industry funding panel would particularly like you to comment on whether the sequence of the digested proteins will affect whether they can assemble into a useful structure for use in a biomaterial in each case.

2. N-Acetylneuraminase lyase (NAL) and dihydrodipicolinate synthase (DHDPS) are enzymes that have very similar structures (Figure 1), each being composed of four identical protein chains that are folded as shown below.



*Figure 1: the structures of NAL and DHDPS from E. coli*

NAL and DHDPS catalyse different chemical reactions (Figure 2) in apparently unrelated metabolic pathways.



*Figure 2: Reactions catalyzed by (a) NAL and (b) DHDPS,*

**QUESTION 2 CONTINUED ON NEXT PAGE**

In 2003, Alan Fersht's group in Cambridge used rational design to introduce a mutation into the NAL scaffold to switch the activity toward that of DHDPS. One point mutation (L142R – exchanging an active site leucine for an arginine residue) was sufficient to create an enzyme that had both DHDPS activity and NAL activity.

(a) (7 marks)

Describe the common structural features of NAL and DHDPS. To what extent are these features typical of metabolic enzymes? How do we know?

(b) (4 marks)

The sequences of NAL and DHDPS show only 24% sequence identity. What does this tell you about the conservation of sequence within structurally related protein families?

(c) (5 marks)

Examine the reaction catalysed by each enzyme, described in Figure 2. Are you surprised that the enzymes that catalyse these reactions have a similar structure? Justify your answer.

(d) (4 marks)

In the conclusion for the manuscript, the authors comment on their creation of a dual function enzyme as follows: "*Perhaps, nature has exploited the catalytic promiscuity of many enzymes to evolve novel enzymes or biological pathways during the course of evolution.*" Do you believe this supposition is likely? How might you test such a hypothesis?

3. Answer **ALL** of the following short answer questions.
- (a) (5 marks)  
Describe the Histone Code Hypothesis.
  - (b) (5 marks)  
How do histones “bend” DNA?
  - (c) (5 marks)  
It is said that Histone Code replication is based on a distributive model. Why does the evidence fit a distributive model?
  - (d) (5 marks)  
Discuss how the Histone Code might have implications for animal cloning.
4. Answer **ALL** of the following short answer questions.
- (a) (5 marks)  
There are, broadly speaking, two kinds of post-translational modification: the addition to, or subtraction of, molecules from the primary structure of the polypeptide. What is the difficulty in determining the number and types of different protein isoforms, and even in completing the survey of possible kinds of isoforms?
  - (b) (5 marks)  
Describe, in detail, how post-translational modification can influence two different kinds of protein isolation procedures.
  - (c) (10 marks)  
“This study shows that human brain and CSF PrP<sup>C</sup> exist under full-length and truncated species that exhibit variable degrees of glycosylation, giving rise to over 60 charge isomers.” Explain this statement with reference to your answers above. Then discuss why it was a novel statement about prions, and why it is of general significance.

**END OF PAPER**