1. A (25 pnts). Starting from succinate and pyruvate write out the sequence of reactions required to metabolize 1 mole of pyruvate and make 3 moles of carbon dioxide.
Provide a **balanced** equation for each reaction giving the **chemical structures** of each of the metabolites (names for reduced credit) **names of the responsible enzymes.** Use the conventional acronyms for **cofactors and prosthetic groups.** Do NOT give the detailed mechanism for the individual enzymes.

e.g. in words.

1. succinate + Q <==> fumarate + QH_2 succinate deh. prosthetic grp = FAD

2. fumarate to malate; fumarase

3. malate to OAA: malate deh. cosubstrate = NAD

4. pyruvate to acetyl CoA; pyruvate deh. complex, cosub = NAD & CoA; prosthetic grps = TPP, FAD & lipoic acid

5. acetyl CoA + OAA to citrate + CoA; citrate synthase, cosubstrate=CoA (write the reaction in the reverse direction).

6. citrate to isocitrate; aconitase, prosthetic grp = 4Fe4S

7. isocitrate to aKg; isocit deh., cosubstrate = NAD; prosthetic grp = Mn

8. aKg to succinyl CoA; aKg deh. complex, cosub = NAD & CoA; prosthetic grps = TPP, FAD & lipoic acid.

Stop HERE -all CO2 has been evolved.

1. B (10 pnts). In separate experiments fresh pigeon flight muscle is incubated with the following compounds radio-labeled as indicated. Indicate what metabolic **events** must occur before the radio-label is found in carbon dioxide.

a) ^{14}C carboxyl-labeled pyruvate.

The pyruvate dehydrogenase rxn.

b) ^{14}C methyl-labeled pyruvate

The pyruvate dehydrogenase rxn. + 3 revolutions of the TCA cycle.

A pyruvate methyl needs 2 revolutions to become a OAA carboxyl and becomes CO2 on the third revolution. (TA-check this).

c) ^{14}C carboxyl-labeled succinate.

1 revolution of the TCA cycle

d) ^{14}C malate-labeled in the secondary alcohol.

Released on the third revolution of the cycle. First rev puts label on the 2 middle C of OAA, 2'nd rev moves label to COOH of OAA. 3'rd revolution releases it as CO2,.

e) ^{14}C malonate-labeled in the methylene group.

Malonate isn't metabolized by any pathway we've considered.

2). What are anapleroptic reactions? Provide one example (using balanced equations) from mammals and a second from plants. What processes (metabolic or otherwise) make anapleroptic reactions necessary? Give 3 examples.

Anapleroptic reactions are those reactions that supply citric acid cycle intermediates.

Examples: Mammals-any CO2 fixation reaction.
Plants: glyoxylate cycle

Necessary because processes remove TCA intermediates either via decomposition of OAA or by supplying intermediates for other metabolic processes. Any 3 of the several examples given in the notes

3. Match the items in the two columns using a notation like: a⇒**1**. Do not assume that all entries on the right must be used up.

a) Can transfer 1 or 2 electrons: **a**⇒ 5	1) NAD^+
b) Introduces CO_2 into a CoA ester: **b**⇒ none	2) Coenzyme B_{12}
c) Can transfer a 2-carbon fragment: **c**⇒ 3	3) Thiamin pyrophosphate
d) Interchanges substituents on adjacent carbons: **d**⇒ 2	4) Lipoic acid
e) Transfers a hydride ion: **e**⇒ 1	5) FAD
f) Reacts with oxygen: **f**⇒ 5	6) Coenzyme A

Which of the entries in the right hand column are:

Cosubstrates: 1, 6
Prosthetic Groups: 2,3,4,5.

4) (a) What is the physical reason that the melting point of octadecanoic acid (18:0) is 63°C and octadecenoic acid (18:1) is 16°C?

18:0 can pack tightly and the cohesive forces between molecules produces a solid.
18:1 has a "bend" because of the double bond-the cohesive forces are weakened and a liquid results

(b) What is the structure (at pH 7) of phosphatidic acid that contains the above two fatty acids Write out the structure in full except that the **alkyl** side-chain of each fatty acid can be replaced by its name or number.

put 18:0 at C1, 18:1 at C2 and phosphate at C3. The phosphate should have a negative charge of 1.5

(c) Provide a simple test to establish whether-or-not a protein is an integral membrane protein.

Do you need a detergent to solubilize it?

(d) An integral protein is known to form a transmembrane pore. How would you determine whether this pore is constructed from helices or from beta sheets.

A hydropathy plot will exhibit several (>6) strong peaks; a beta barrel should have none

(e) What is the difference between primary and secondary active transport?

Primary: Driven by electron transport (mitos or chloroplasts) or ATP hydrolysis; makes a proton gradiennt.

Secondary: transport of most metabolites by this proton gradient.

(f) Bacteria accumulate lactose by lactose+H^+ symport and acetate by acetate+H^+ symport. For the same magnitude of proton motive force across the membrane will lactose and acetate be concentrated to the same extent? Explain!.

No-lactose uses Delta P while acetate uses only Delta pH-the former will be conc. to a larger extent.

(g) To what extent are the adrenaline receptor and acetyl choline receptor similar? To what extent are they different (ignoring the fact that they undoubtedly have different protein structures)?

Similarites: Both intrinsic proteins
Both bind ligands and initiates a biochemical process.

Differences: Liganded AR migrates to G protein and causes a ADP/ATP exchange on G-alpha

AChR: A channel opens to allow ion flow across the post-synaptic membarne

5.) The proton-motive force (ΔP) across the mitochondrial membrane is typically -200 millivolts; about 75% is due to $\Delta\varphi$ and 25% due to ΔpH.

What would be the value of the proton-motive force following treatment of mitochondria with:

(Explain your responses.)

1) Valinomycin

-200. Equilibrates K; no effect

2) Gramicidin.

0: Equilibates everythiing; kills Delta P

3) Dinitrophenol (DNP)

0: Equilibates protons; kills Delta P

4) Tetraphenylphosphonium (TPP^+)

-200: responds to delta phi without changing it.

5) 5,5-dimethyl-2,4-oxazolidinedione (DMO).

-200: repsonds to delta pH without changing it.

Some bacteria use a "sodium motive" force with the same magnitude and relative composition for $\Delta\varphi$ and ΔpNa as given above for ΔP. What would the value of this force after treatment of the bacteria with:

(Explain your responses).

1) Valinomycin

-200: Equilibrates K; no effect

2) Gramicidin.

0: Equilibates everythiing; kills Delta Na

3) Dinitrophenol (DNP)

-200: Equilibates protons; no effect

4) Tetraphenylborate (TPB^-)

-200: responds to delta phi without changing it.

5) 5,5-dimethyl-2,4-oxazolidinedione (DMO).

-200: repsonds to delta pH -no effect