

C483 Exam 1
Spring 2016

Name Key _____ Seat Number _____

Student ID _____ AI _____

The last page of this exam contains pKa values and other information you might find useful.

This exam contains 110 points. The highest score you may earn on this exam is 100 points.

1. _____/20pts

2. _____/10pts

3. _____/20pts

4. _____/10pts

5. _____/10pts

6. _____/10pts

7. _____/10pts

8. _____/10pts

9. _____/10pts

Total:

Regrading: All requests for regrades must be submitted in writing within 48 hours of the return of the exam. You must explicitly state what has been misgraded and why it is an error. The entire exam will be regraded, which could result in points being added or deducted overall.

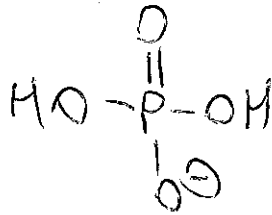
Section 1: Reading guides (50 points)

1. 20 pts. Fill in the blanks (2 points each.)

A. Nucleic acids are polymers of nucleotides held together by the phosphodiester linkage (bond.)

B. If a carbonyl has been transformed into an alcohol, the carbon atom has been reduced (reduced/oxidized), and this reaction is generally not spontaneous (spontaneous/not spontaneous.)

C. Draw the major ionization state of phosphoric acid at pH 5.



D. Carbonic acid/bicarbonate can serve as a biological buffer even with its low pH because the system is open.

E. H-bonding is a stronger intermolecular force than (dipole/dipole) - induced dipole.

F. If the template strand of a gene has a 3'-ATG-5' sequence, the mRNA will have a 5' → 3' sequence of



G. Arg⁺, Lys is an amino acid that is positively charged at almost all physiological pHs.

H. When an allosteric protein binds its ligand well, the equilibrium lies toward the relaxed state.

I. Actin^o, tubulin is an example of a structural protein that contains NTP binding sites.

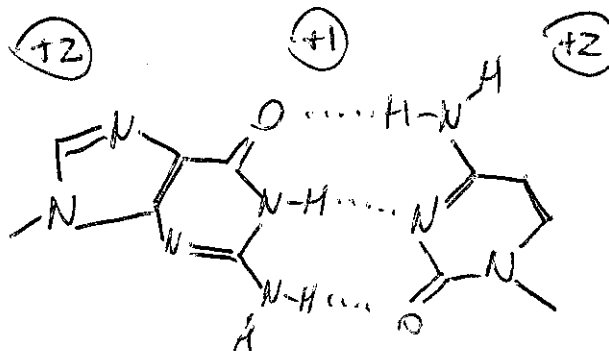
J. When binding of a substrate to an enzyme causes a conformational shift in the enzyme that makes it bind substrate tightly, it is called cooperativity or induced fit.

2. 10 pts. True or false (1 point each)

- A. True Amino acids with the abbreviations L, I, V, and W are all considered hydrophobic amino acids.
- B. False Breaking a disulfide bond into two cysteine residues is a hydrolysis reaction.
- C. True The alpha helix is a right-handed structure which is highly polar.
- D. False The interior of a protein is often regular in its secondary structure because secondary structures tend to have no ionizable amino acids.
- E. True The curve for a myoglobin oxygen binding curve is hyperbolic.
- F. False The increase of hemoglobin's oxygen binding ability when the pH decreases is known as the Bohr Effect.
- G. False Kinesin is a processive motor because it completely releases from its filament before reattaching.
- H. False Chymotrypsin uses its oxyanion hole to make the attacking nucleophile more reactive.
- I. True The second pKa of a polyprotic acid is always higher than its first pKa.
- J. False GC rich DNA strands are harder to separate because GC pairs form more H-bonds.

3. 20 pts. Short answer (5 points each)

A. Draw the nucleobases of the GC base pair and indicate the hydrogen bonds.



B. What percentage of an imidazole buffer at pH 7.6 is in its deprotonated form?

$$pH = pK_a + \log \frac{A^-}{HA}$$

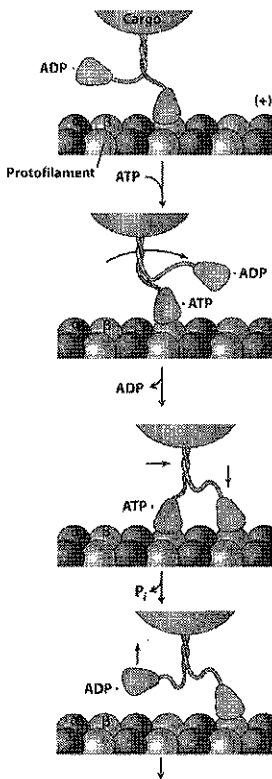
$$\% A^- = \frac{4}{4+1} = 80\%$$

$$7.6 = 7.0 + \log \frac{A^-}{HA}$$

$$\textcircled{+3} \quad 4.0 = \frac{A^-}{HA}$$

$\textcircled{+2}$

C. Write a stepwise mechanism for this motor protein based on the figure provided.



$\textcircled{+2}$
ATP binding to lead foot throws lagging foot forward

$\textcircled{+1}$
Release of ADP allows new lead foot to bind

$+3$
Hydrolysis of ATP released lagging foot (release of P_i)

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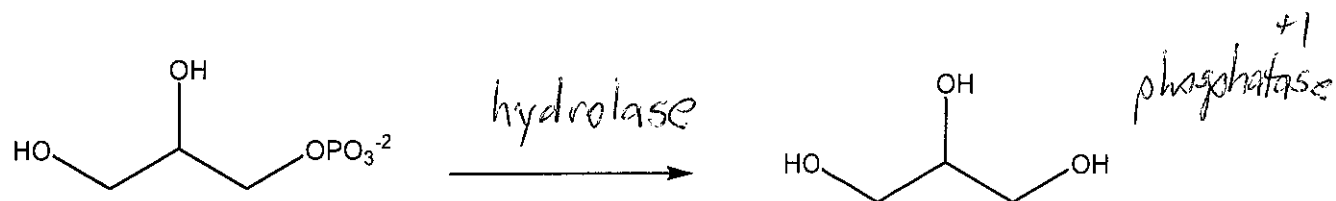
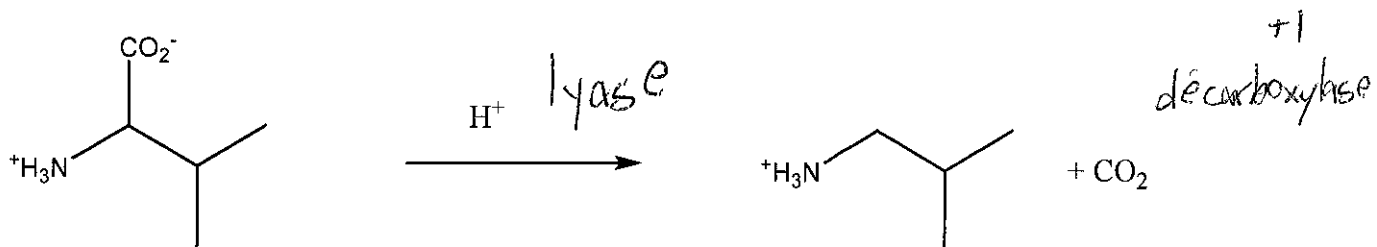
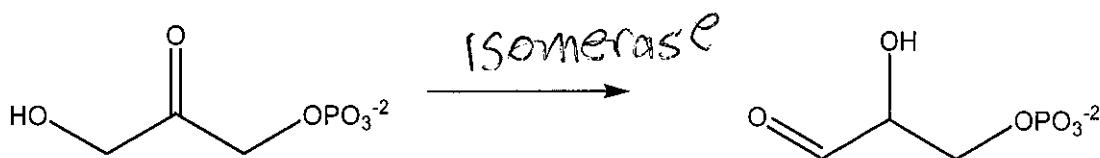
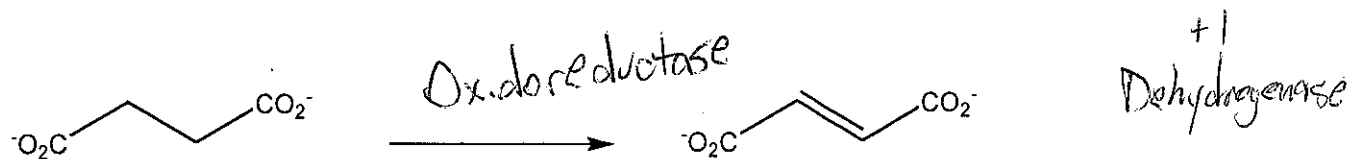
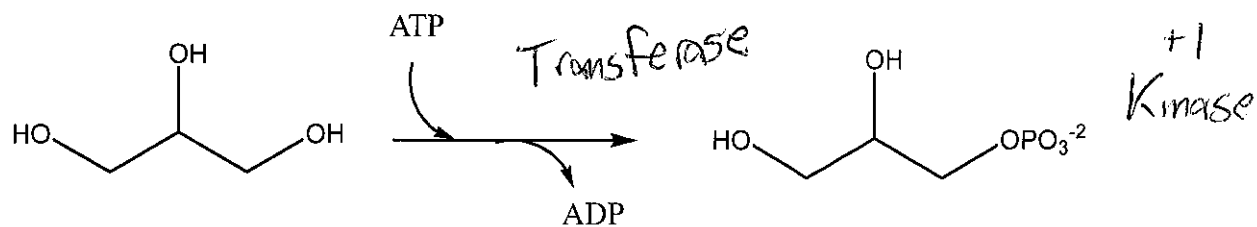
D. Write a sequence of the portion of the coding strand of a gene that will produce the peptide sequence His-Trp-Cys.

	<u>His</u>	<u>Trp</u>	<u>Cys</u>
5'	CAT	TGG	TGT
	or		or
	CAC		TGC

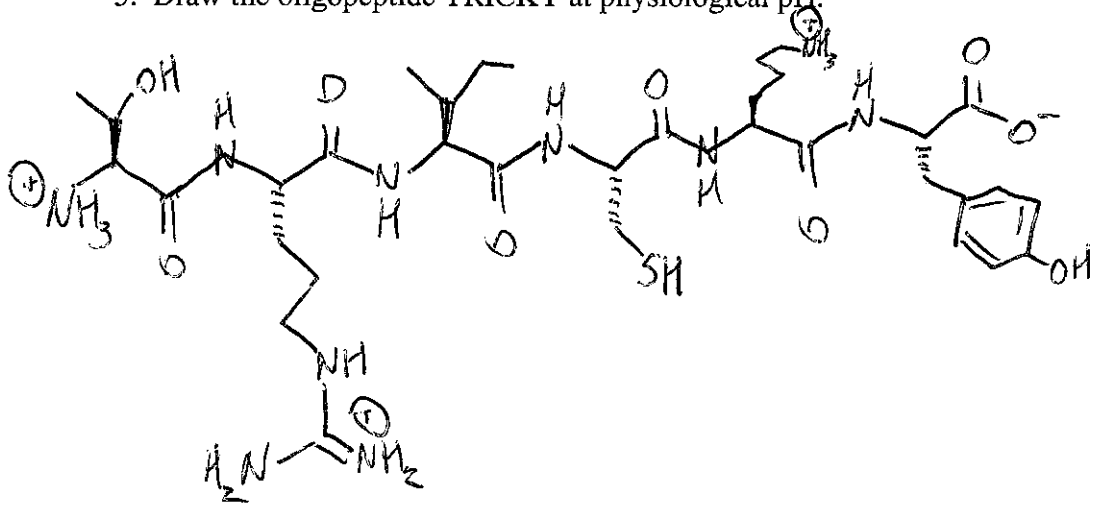
5' CAT TGG TGC 3'

Section 2: Problems (10 points each)

4. Label each of the reactions below with the class of enzyme that would catalyze it.

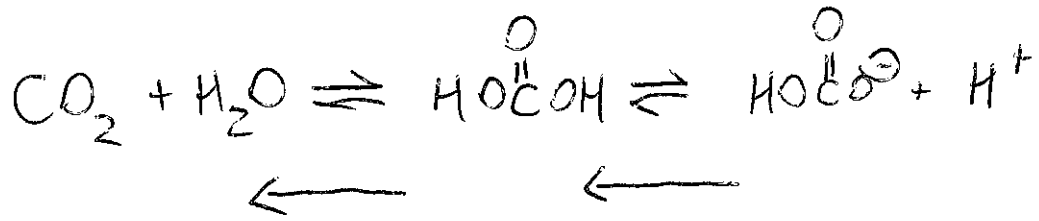


5. Draw the oligopeptide TRICKY at physiological pH.



- Backbone (+2)
- Stereochem (+1)
- Sidechains (+6)
- ionization (+1)

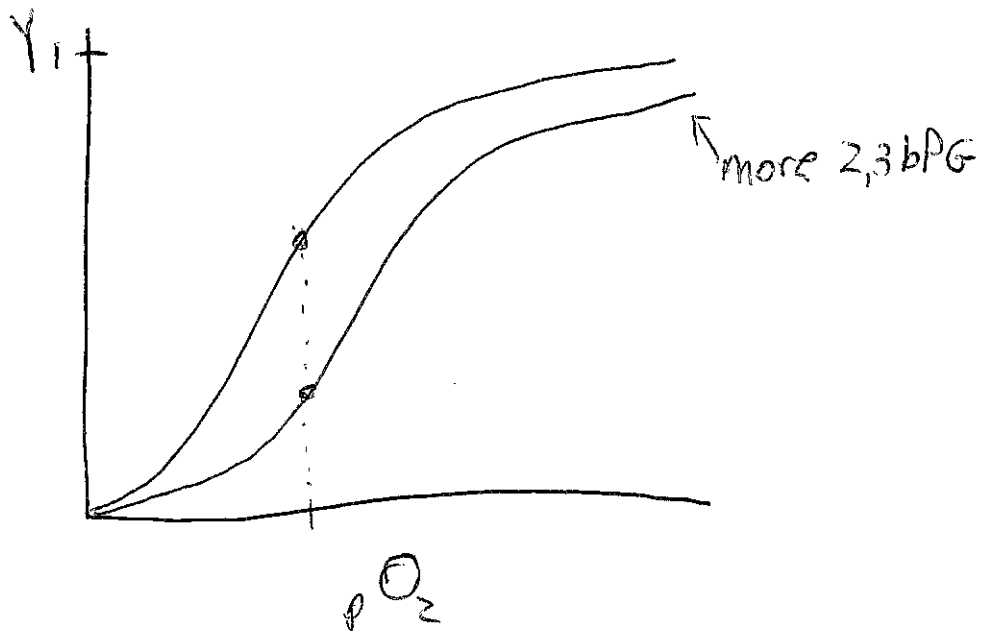
6. People who live at or near sea-level undergo high-altitude acclimation when they go up to 5000 m. As they begin to hyperventilate to gain more oxygen, they also expel more CO₂. How would this effect blood pH? Explain with reference to appropriate chemical reactions.



(+4)

Expelling CO₂ pulls these equilibria to the left, meaning bicarb reacts with acid to raise pH.

After a few weeks, these people start to produce more 2,3-bisphosphoglycerate. Explain how this aids in acclimation by drawing an appropriate oxygen binding graph for hemoglobin.



(+4)

(+2) More 2,3bPG shifts equilibrium toward Tense, meaning Hb has lower binding affinity. Hb releases more oxygen to deprived muscle/tissue.

7. One liter of a 0.10 M Tris buffer is prepared and adjusted to a pH of 8.2.

A. What are the concentrations of the conjugate acid and weak base at pH 8.2?

$$\text{pH} = \text{p}K_a + \log \frac{A^-}{HA}$$
$$8.2 = 8.3 + \log \frac{A^-}{HA}$$
$$10^{-.1} = \frac{A^-}{HA} = .79$$
$$\% A^- = \frac{.79}{1.79} = 44\%$$

$[A^-] = 0.044 \text{ M}$
 $[HA] = 0.056 \text{ M}$

 (+4)

B. If 1.5 mL of 3.0 M HCl is added to the buffer, what is the new pH?

$$3.0 \frac{\text{mol}}{\text{L}} (0.0015 \text{ L}) = .0045 \text{ mol HCl}$$

$$\text{new } [A^-] = 0.044 - 0.0045 \text{ mol} = 0.0395 \text{ mol}$$

$$\text{new } [HA] = 0.056 + 0.0045 \text{ mol} = 0.0605 \text{ mol}$$
 (+4)

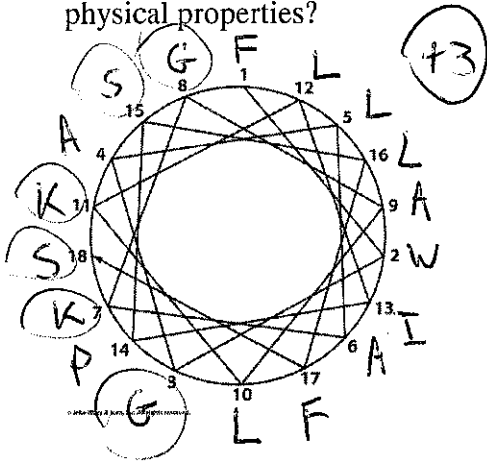
$$\text{pH} = \text{p}K_a + \log \frac{A^-}{HA}$$

$$\text{pH} = 8.3 + \log \frac{[.0395/1.0015] \frac{\text{mol}}{\text{L}}}{[.0605/1.0015] \frac{\text{mol}}{\text{L}}} = 8.1$$
 (+2)

8. A 24-residue peptide called Pandinin 2 was isolated from scorpion venom and found to have hemolytic properties. (It ruptures red blood cells.) The sequence of the first 18 residues is shown below.

FWGALAKGALKLIPSLFS

A. Use this helical wheel to plot the sequence of this helix. What does this suggest about its physical properties?

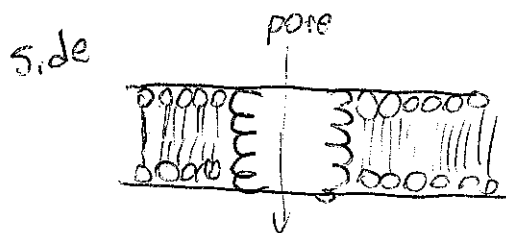
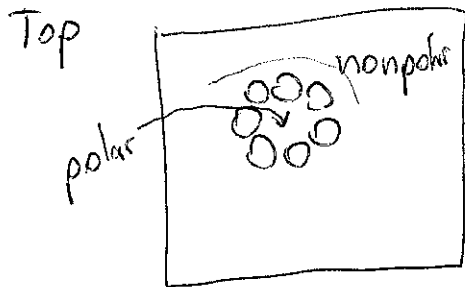


This helix is amphipathic

43

B. An 18-residue helix is perfectly suited to span a lipid bilayer. Draw a schematic of a lipid bilayer with Pandinin 2, and explain with reference to intermolecular forces, how this protein will lyse cells.

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Hydrophobic effect - half of α helix lines up with lipid bilayer through VDW forces. The polar/charged groups line up with center of pore to make a hydrophilic hole in the cell.

Section 3: Case study (10pts) In an effort to develop mutants of Hemoglobin with altered oxygen binding abilities, a team of scientists has begun to investigate possible mutations.

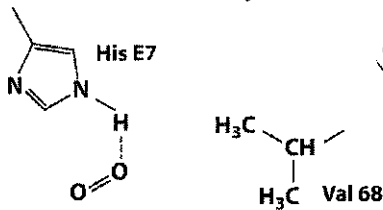
A. First, they collected the sequences of various known hemoglobins, found in the table below.

Position	Human	Chicken	Alligator	Turtle	Tuna	Carp
1	D	D	K	D	D	D
2	I	I	L	L	Y	F
3	P	A	P	S	T	E
4	G	G	E	A	T	E
5	H	H	H	H	M	T
6	G	G	G	G	G	G
7	Q	H	H	Q	G	G
8	E	E	E	E	L	E
9	V	V	V	V	V	V
10	L	L	I	I	L	L

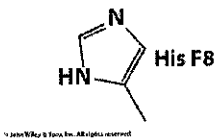
They proposed the following three mutants of human hemoglobin: I2→N2, G6→A6, and E8→D8. Which would you expect to be the most likely to be functional hemoglobin? Explain.

- (42) I2 → N2 - not likely - major change from hydrophobic to polar
- (42) G6 → A6 - not likely - G6 appears to be invariant.
- (42) E8 → D8 - most likely - E/D mutation maintains anionic/polar group

B. Val-68 plays an important role as a boundary of the hydrophobic heme pocket. This group of scientists expect that both the V68→S68 and V68→I68 mutants would decrease activity based on the structure they obtained (below.) Explain their reasoning for each mutation.



(42) V68 → S68 would make cavity more polar



(42) V68 → I68 would be bigger and potentially block O₂ binding site (sterics)

Data Tables

Amino acid pKa values

C-terminal	3.1
N-terminal	8.0
Aspartate, glutamate	4.1
Histidine	6.1
Cysteine	8.3
Tyrosine	10.9
Lysine	10.8
Arginine	12.5

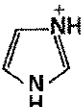
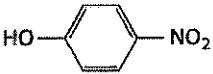

TABLE 3-3 The Standard Genetic Code^a

First Position (5' end)	Second Position								Third Position (3' end)
	U		C		A		G		
U	UUU	Phe	UCU	Ser	UAU	Tyr	UGU	Cys	U
	UUC	Phe	UCC	Ser	UAC	Tyr	UGC	Cys	C
	UUA	Leu	UCA	Ser	UAA		UGA		A
	UUG	Leu	UCG	Ser	UAG		UGG	Trp	G
C	CUU	Leu	CCU	Pro	CAU	His	CGU	Arg	U
	CUC	Leu	CCC	Pro	CAC	His	CGC	Arg	C
	CUA	Leu	CCA	Pro	CAA	Gln	CGA	Arg	A
	CUG	Leu	CCG	Pro	CAG	Gln	CGG	Arg	G
A	AUU	Ile	ACU	Thr	AAU	Asn	AGU	Ser	U
	AUC	Ile	ACC	Thr	AAC	Asn	AGC	Ser	C
	AUA	Ile	ACA	Thr	AAA	Lys	AGA	Arg	A
	AUG	Met	ACG	Thr	AAG	Lys	AGG	Arg	G
G	GUU	Val	GCU	Ala	GAU	Asp	GGU	Gly	U
	GUC	Val	GCC	Ala	GAC	Asp	GGC	Gly	C
	GUA	Val	GCA	Ala	GAA	Glu	GGA	Gly	A
	GUG	Val	GCG	Ala	GAG	Glu	GGG	Gly	G

^aThe 20 amino acids are abbreviated; Ala, alanine; Arg, arginine; Asn, asparagine; Asp, aspartate; Cys, cysteine; Gly, glycine; Gln, glutamine; Glu, glutamate; His, histidine; Ile, isoleucine; Leu, leucine; Lys, lysine; Met, methionine; Phe, phenylalanine; Pro, proline; Ser, serine; Thr, threonine; Trp, tryptophan; Tyr, tyrosine; and Val, valine.

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TABLE 2.4 pK Values of Some Acids

Name	Formula ^a	pK
Trifluoroacetic acid	CF ₃ COOH	0.18
Phosphoric acid	H ₃ PO ₄	2.15 ^b
Formic acid	HCOOH	3.75
Succinic acid	HOOCCH ₂ CH ₂ COOH	4.21 ^b
Acetic acid	CH ₃ COOH	4.76
Succinate	HOOCCH ₂ CH ₂ COO ⁻	5.64 ^c
Thiophenol	C ₆ H ₅ SH	6.60
Phosphate	H ₂ PO ₄ ⁻	6.82 ^c
N-(2-acetamido)-2-aminoethanesulfonic acid (ACES)	H ₂ NCOCH ₂ NH ₂ ⁺ CH ₂ CH ₂ SO ₃ ⁻	6.90
Imidazole		7.00
p-Nitrophenol		7.24
N-2-hydroxyethylpiperazine-N'-2-ethanesulfonic acid (HEPES)	HOCH ₂ CH ₂ NH ⁺  NCH ₂ CH ₂ SO ₃ ⁻	7.55
Glycinamide	⁺ H ₃ NCH ₂ CONH ₂	8.20
Tris(hydroxymethyl)aminomethane (Tris)	(HOCH ₂) ₃ CNH ₂ ⁺	8.30
Boric acid	H ₃ BO ₃	9.24
Ammonium ion	NH ₄ ⁺	9.25
Phenol	C ₆ H ₅ OH	9.90
Methylammonium ion	CH ₃ NH ₃ ⁺	10.60
Phosphate	HPO ₄ ²⁻	12.38 ^d

^aThe acidic hydrogen is highlighted in red; ^bpK₁; ^cpK₂; ^dpK₃.

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