No Analytical crib available
September 17, 2016
Written by Professor Wirth
Ph# 45328
The dsDNA tailed bacterial phages are most abundant life forms on earth. Please answer the following questions about their structural and functions.

1) (15 points) The phage head contains high density of dsDNA genome. A commonly used method to release the genome is to add EDTA to the samples.
   a) What is the major molecular interaction involved in this process? (5 points)
      EDTA chelating Mg2+ and Electrostatic repulsion of negatively charged DNA
   b) Explain the principal of this approach. (10 points)
      • Mg2+ ions trapped in the packed dsDNA inside the phage capsid will reduce the repulsion forces from the negatively charged DNA
      • EDTA binds Mg2+ ions which reduces the amount of trapped Mg2+
      • The increased repulsion force from the packed dsDNA will force the release of dsDNA out of the protein capsid

2) (40 points) Molecular interactions we commonly cited can all be considered as special situations of the more fundamental force, electromagnetic force. Please first define and then explain each of the following interactions using this principal.
   a) salt bridge (10 points)
      Attractions between positively charged amino acid side chains and negatively charge amino acid side chains.
   b) pi-stacking (10 points)
      Parallel arrangement of aromatic side chains in protein structures. The electron distribution of the aromatic amino acid sidechains is approximately negative in the center and positive around the edge. When two aromatic sidechains are close to each other, they tend to arrange in parallel with lateral offset or in perpendicular with edge of one aromatic sidechain pointing towards the center of the other aromatic sidechain.
   c) H-bond (10 points)
      When H is covalently bonded to electron negative atoms in protein (O and N), the two bonded atoms can be approximated as a permanent dipole consisting of positive H and negative O/N atoms. When two such dipoles are close to each other, the dipole-dipole interactions tend to align them in head-to-tail arrangement with a H atom positioned between two O/N atoms.
   d) van del Waals (10 points)
      Weak attractions between two neutral atoms due to the interactions between the transient induced dipoles. The neutral atoms can have transient anisotropic electron cloud distribution that can be approximated as a weak
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Such transient dipole can induce its neighbor atoms to also have transient anisotropic electron cloud distribution and thus dipole. Such mutual induction of transient dipoles by two neighboring neutral atoms is the basis of the van der Waals interaction.

3) (25 points) A surprising findings a few years ago for the major capsid structure of the dsDNA tailed phages is that the capsid structures share a common fold even for phage hosts across all three life domains.
   a) What conclusion can you draw from these observations? (10 points)
      The phages have a common ancestor that appeared before the three domains of lives separated
   b) What will be your predictions of the similarities of the phage capsid protein sequences? (5 points)
      The sequences are also conserved but might be much less than the conservation level of the protein fold
   c) Justify your prediction of the sequence similarities and relate that to the observation of common protein fold. (10 points)
      The protein fold needs to be well conserved to maintain its essential function in protecting the genome. Altered protein fold that fails to form robust capsid and protect the genome will be evolutionally discarded. However, the sequences can mutate and diverge more as many mutations would not alter the protein fold and thus were retained. As a result, many tailed dsDNA phages with undetectable level of sequence similarity still share the same protein fold.

4) (20 points) Scientists have been trying very hard to obtain the phage structures but could only do that in recent years. Use your knowledges of structural determination methods to explain:
   a) Why did we fail to obtain the phage structures if many virus structures could already be solved in the 80s? (10 points)
      In the past X-ray crystallography was the only method that can determine structures as large as the phages. As many viruses with rigid and simpler icosahedral capsid could be crystallized, their structures could be solved by X-ray crystallography since early 80s. However, the complicated large phage structures with head and tail were too difficult to crystallize and thus the phage structures could not be determined using X-ray crystallography.
   b) Why can we solve the phage structure now routinely? (10 points)
      In recent years, single particle cryo-EM has seen dramatic progresses and it can routinely solve structures of macromolecular complexes and viruses including dsDNA tailed phages to nearly atomic resolutions to allow reliable atomic modeling.
Answer Key
Inorganic Chemistry Cumulative Exam
Purdue University
September 17, 2016

Question 1:
A) Phytoplankton growth in the Southern Ocean is not limited by N or P.
B) Fe. That is what is limited there. (Not the case in other waters.)

Question 2:
Add some organic “shrubbery” to prevent the hemes from coming close together enough to “rust” via Fe-O-Fe bonds.

Question 3:
A) Something with an HO-ZnN\textsubscript{3} type of structure would be nice.
B) It’s not easy. But it could work. Some models do.
C) Maybe make the Zn-OH nucleophile more nucleophilic by, for example, adding electronic density by making one of the neutral N ligands an anionic O donor.

Question 4:
The zinc forms a loop structure that sticks up from the protein backbone and looks like a finger pointing up.

Question 5:
You have all of your eggs in one basket- only one compound. And you are only showing the killing of cancer cells. You need to show specificity.
1) tri-n-butyl CF$_3$SO$_3$- [Sb$_3$] -

TBAP Bu$_4$N$^+$ F$^-$

2) Roberts experiment was to

\[
\text{label with} \quad ^{13}C
\]

\[
\text{N}_2\text{H}_4
\]

3) \[
\text{Bulii} \quad (\text{86 Mg})
\]

4) CO$_2$
5) Me₂Si results were "inconsistent" in formation of the silane. Presumably a steric issue since they used very bulky aromatic halides and about generation of benzyn.
Physical chemistry

$H \Psi(R, R') = E(R) \Psi(R, R')$

Bom-Oppenheimer\ approximation

$\frac{\partial E}{\partial R} = 0$

$E_{FR}$

$R_{eq}$

(a)

(b)

Overlap

$\Psi_{1s}$

$\Psi_{1s}$

(c)

$1s^2 \xrightarrow{R \to 0} \text{He atom}$

1) Excited

$\text{He}$

$\text{He}$
(2) \( \psi(x,t) = \psi(x) e^{-iEt/h} \)
\[
\left| \psi(x') \right|^2 = \left| \psi(x) \right|^2
\]

(b) Perturb then Solve Using Interactive Picture

(c) \( \psi(y_1, y_2) = -\psi(y_2, y_1) \) \text{ antisymmetric wave function}
\[
\psi(1, 2) = -\psi(2, 1)
\]

(3) \( V(x) \quad 0 < x < \frac{\hbar}{m} \)

(b) \[ \hat{H} \psi_n(x) = E_n \psi_n(x) \]
\[
\frac{\partial^2}{\partial x^2} = 0 \quad \Rightarrow \quad E(x) = E(x_{opt})
\]
\[
\psi_n(x) = N e^{-\frac{1}{2m} x^2 x^2} \quad x_{opt} = \frac{\hbar}{m} \]

(c) \[ V(y) \quad \text{No} \]

(d) \[ F = -\frac{dv}{dx} = -2x \quad \text{Linear} \]