Topic: Applying Chemistry Knowledge: A Semester in Review

A look back at the course objectives: My goal is for 5.111 students to have a working knowledge of chemical principles that will allow them to:

• take advanced chemistry classes; carry out a UROP in the chemistry department; employ chemistry in research outside of the chemistry department
• appreciate how chemistry is used to solve real-world problems
• make informed decisions about personal health, environmental and energy issues, and science policy
• advance science and engineering through the application of chemical principles.

A look back at the course topics:
Atomic theory
Periodic Table Trends Basic properties of matter
Bonding Structure of Molecules
Thermodynamics
Chemical Equilibrium & Solubility
Acid-Base
Oxidation-Reduction How matter reacts
Transition Metals Kinetics

Let's review selective topics using carbon dioxide as a case study.
CO₂ is a waste product of the combustion of fossil fuels. It is a greenhouse gas and thus a player in global warming. It also contributes to the acidification of our oceans. We need to remove it from our environment, but what if we can do one better; use it to make biofuels?

Approaches Include: designing small molecule catalysts to convert CO₂ to biofuels and re-engineering biological CO₂ fixation pathways, but before either we do either, we must understand the basic properties and reactivity of our reactant – CO₂.

Basic Properties of CO₂
BONDING. How is C bonded to O in CO₂? Let’s use Lewis structures to make a prediction.

STRUCTURE. What is the geometry a CO₂ molecule? And what is its polarity?
Reactivity of CO₂
THERMODYNAMIC. Is CO₂ stable or unstable compared to its elements?

\[ \text{C}_\text{gr} (s) + \text{O}_2 (g) \rightarrow \text{CO}_2 (g) \]

To answer this question, one needs to know__________________.

Given that __________ is -394.39 kJ/mol, CO₂ is ________________.

Let’s review what we have learned about CO₂. It has __________bonds, which typically means a big bond dissociation energy.

It is __________________, ____________________ and ____________________.

With knowledge of our reactant in hand, we next seek to understand how nature “fixes” carbon dioxide (i.e. converts one-carbon units into multi-carbon units). There are six pathways that fix CO₂. One pathway of interest is the microbial acetogenesis pathway.

In acetogenesis, two molecules of CO₂ are added to coenzyme A (CoA) to make acetyl-CoA (a precursor to several multicarbon molecules that can serve as biofuel).

\[
\begin{align*}
\text{CO}_2 & \rightarrow \text{CH}_3^+ \\
\text{CO}_2 & \rightarrow \text{CO}
\end{align*}
\]

Before scientists can harness microbial acetogenesis to make biofuels, they must understand how it works. Does acetogenesis require redox reactions? Are some of the reactions acid-base catalyzed? Are transition metals involved? What are the challenging or rate-limiting steps? Which factors influence the chemical equilibrium of each reaction?

OXIDATION-REDUCTION. Is CO₂ being reduced or oxidized?__________________.

CO₂ is converted to CH₃⁺ through the action of five different enzymes. How are these carbon units transferred in an efficient manner from enzyme to enzyme? Answer: by attaching them to B vitamin folate (or folic acid) and having the folate shuttle between enzymes.

Folate is a wonderful vehicle for transferring one-carbon units, but after CO₂ is fully reduced to a methyl moiety (CH₃⁺), how is it removed from the folate?

ACID-BASE. Removal of CH₃⁺ from folate requires that folate is protonated. If the pKₐ of folate is 4.8, how much will be protonated at physiologically pH?

[Diagrams of deprotonated and protonated folate]
Removal of the methyl group is challenging given the low pK<sub>a</sub> of the folate. How is this challenge overcome? Answer: nature uses a vitamin B<sub>12</sub> dependent enzyme.

**TRANSITION METALS AND CATALYSIS.** Methyl transfer from folate has a big E<sub>a</sub> barrier. To catalyze this reaction, the highly reactivity +1 oxidation state of an enzyme-bound vitamin B<sub>12</sub> is used. Enzyme-bound B<sub>12</sub> removes the methyl group from folate, forming methylB<sub>12</sub>.

\[
pH = pK_a - \log \left( \frac{[HA]}{[A^-]} \right) \quad 7.4 = 4.8 - \log \left( \frac{[HA]}{[A^-]} \right) \quad \frac{[HA]}{[A^-]} = \]

Geometry around Co: dentate ligand
CHEMICAL EQUILIBRIUM
The $\text{B}_{12}$ enzyme exists in both OPEN and CLOSED conformations. These conformations are in equilibrium with each other.

The CLOSED state protects the highly reactive $\text{B}_{12}$ and the OPEN state allows the $\text{B}_{12}$ enzyme to accept the methyl group from a folate molecule, which is bound to a dimeric methyl transferase enzyme ($\text{MeTr}_2$).

The OPEN state also allows for the $\text{B}_{12}$ enzyme to donate the methyl group to the enzyme that makes acetyl-CoA (acetyl-CoA synthase).

Next, the $\text{B}_{12}$ enzyme must open up again to transfer the methyl group to the enzyme that makes acetyl-CoA. The equilibrium of conformers of the $\text{B}_{12}$ enzyme is shifted when the other enzymes and/or the other reactants (like folate) bind.

Enzymes are dynamic.
Chemistry is dynamic.
CHEMISTRY IN SOLUTION IS COOL!!!!!
AND CAN SAVE THE PLANET!!!!!!!