Professional Scientific Societies for Toxicology

- Society of Toxicology (SOT)
  - http://www.toxicology.org/

- Society of Environmental Toxicology & Chemistry (SETAC)
  - http://www.setac.org/

Goal of Environmental Toxicology

- Predict the effects or impact of chemical technologies on organism (ecosystems)

Conceptual Frameworks for Understanding Fate & Effect of Environmental Contaminants

- Environmental Chemodynamics
- Toxicodynamics

The Logical Process for Determining Likelihood of Effects

- Risk Assessment
  - Hazard Identification
  - Dose-response characterization
  - Exposure assessment
  - Risk characterization

What Is Needed to Estimate (Guess) The Risk?

Risk Assessment

Toxicology

Environmental Chemistry

No Observable Effect Level

Exposure Assessment
“Residues”

- Residues refer to chemical contaminants in the physical environment and in biological tissues.
- The constituents of chemical products (or formulations) become residues when they are dispersed into the environment.

Residue Amount

- Expressed as a concentration:
  - Unit of mass per volume or surface area:
    - Milligrams per Liter (mg/L) (or per square meter)
    - Micrograms per milliliter (µg/mL) (or per sq. cm)
  - A proportion:
    - 1% (1 part per 100)
    - 0.0001% (1 part per million)
  - A molar quantity:
    - Moles/L (if in solution)
      - One mole = the molecular weight of a substance in grams
      - 1 µmol = the molecular weight in micrograms

What Does It Mean?

- Usual range of detections many environmental contaminants ranges from ppt (parts per trillion) - ppb (parts per million).
  - From the perspective of purity, that translates to:
    - 99.9999999999% -- 99.9999999%
    - I.e., if 1 ppb = 0.0000001%, then 100% minus 0.0000001% yields 99.9999999%

Analytical Technology Has Advanced Faster Than Biological Understanding

Frequency of Atrazine Detection in Shallow Aquifers Increases as Reporting Limit Decreases

Kolpin et al. JEQ 25 (1996)
Pesticide Residues--
Frequencies/Identities/Concentrations

Relevant Questions
- Method Detection Limit
- Method Quantitation Limit
- Concentrations
  - means
  - medians
  - geometric mean
  - percentiles

General Chemistry Review

Emphasis on Functional Groups
&
The Concept of Polarity

<table>
<thead>
<tr>
<th>Name</th>
<th>Symbol</th>
<th>Atomic Number</th>
<th>Atomic Mass</th>
<th>No. of Electrons in Shell</th>
</tr>
</thead>
<tbody>
<tr>
<td>Helium</td>
<td>He</td>
<td>2</td>
<td>4.003</td>
<td>2</td>
</tr>
<tr>
<td>Carbon</td>
<td>C</td>
<td>6</td>
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<tr>
<td>Nitrogen</td>
<td>N</td>
<td>7</td>
<td>14.007</td>
<td>5</td>
</tr>
<tr>
<td>Oxygen</td>
<td>O</td>
<td>8</td>
<td>15.999</td>
<td>6</td>
</tr>
<tr>
<td>Fluorine</td>
<td>F</td>
<td>9</td>
<td>18.998</td>
<td>7</td>
</tr>
<tr>
<td>Neon</td>
<td>Ne</td>
<td>10</td>
<td>20.180</td>
<td>8</td>
</tr>
<tr>
<td>Phosphorus</td>
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<td>30.974</td>
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<tr>
<td>Sulfur</td>
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<td>16</td>
<td>32.060</td>
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<td>39.948</td>
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<td>Bromine</td>
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<td>79.904</td>
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<td>Krypton</td>
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<tr>
<td>Xenon</td>
<td>Xe</td>
<td>54</td>
<td>131.290</td>
<td>8</td>
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</table>

Electronegativity (EN)

Table 2. Electronegativities of Atoms (the greater the number the greater the EN)

<table>
<thead>
<tr>
<th>Name</th>
<th>Symbol</th>
<th>Charge of Kernel</th>
</tr>
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<tbody>
<tr>
<td>Hydrogen</td>
<td>H</td>
<td>+1</td>
</tr>
<tr>
<td>Helium</td>
<td>He</td>
<td>+2</td>
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<tr>
<td>Carbon</td>
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<td>N</td>
<td>+5</td>
</tr>
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<td>Oxygen</td>
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<td>+6</td>
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<tr>
<td>Fluorine</td>
<td>F</td>
<td>+7</td>
</tr>
<tr>
<td>Neon</td>
<td>Ne</td>
<td>+8</td>
</tr>
<tr>
<td>Phosphorus</td>
<td>P</td>
<td>+5</td>
</tr>
<tr>
<td>Sulfur</td>
<td>S</td>
<td>+6</td>
</tr>
<tr>
<td>Chlorine</td>
<td>Cl</td>
<td>+7</td>
</tr>
<tr>
<td>Argon</td>
<td>Ar</td>
<td>+8</td>
</tr>
<tr>
<td>Bromine</td>
<td>Br</td>
<td>+7</td>
</tr>
<tr>
<td>Krypton</td>
<td>Kr</td>
<td>+8</td>
</tr>
<tr>
<td>Xenon</td>
<td>Xe</td>
<td>+8</td>
</tr>
</tbody>
</table>

* The kernel refers to the nucleus and the inner filled electron shells.

Covalent Bonds

- Formed between atoms by sharing electrons
**Polarity (Polar Bonds)**

- Owing to differences in electronegativity, sharing of electrons in the bonding orbitals may be unequal, i.e., toward one atom or the other.
- Thus, positive (electron deficient) and negative (electron rich) poles are set up between atoms in a molecule.

\[
\begin{align*}
\delta^+ & \quad \delta^- \\
\text{O} & \quad \text{C} \\
\end{align*}
\]

**Ionic Bonding**

- When atoms of very large differences in EN bond, such as between column 7 and column 1 or 2 elements, then the electrons may be transferred from the atoms of lowest electronegativity to the atoms of highest electronegativity.
- Thus, the atoms of highest EN would have a “permanent” negative charge.
- The atoms of lowest EN would have a “permanent” positive charge.

\[
\begin{align*}
\text{Na}^+ & \quad \text{Cl}^- \\
\end{align*}
\]

**Hydrogen Bonding**

- When hydrogen (H) is bonded to O or N, which are more electronegative, then the relatively positive H can be attracted to an electronegative atom on nearby molecules.
- Especially if the more EN atom has an un bonded pair of electrons.
- Forms a hydrogen bond; not as strong as covalent or ionic bond, but it can form stable molecular interactions.

\[
\begin{align*}
\delta^- & \quad \delta^+ \\
\text{O} & \quad \text{H} \\
\end{align*}
\]

**Geometry (Bond Angles)**

- Atoms within molecules actually exist in definite geometric spatial relationships to one another that are characteristic of the type of bond.
- For ex., carbon atoms have four valence electrons, each oriented toward the corner of a tetrahedron.
- Nitrogen often uses three valence electrons (with an unpaired electron available for bonding an electron deficient species like H); its spatial geometry tends to be trigonal.

**Aromatic structures** (alternating double bonds in ringed systems) tend to be planar (i.e., less free rotation of the carbon atoms).
- Characterized by delocalized ‘pi’ electrons that can impart some electronegative character.
- Aromatic structures also are more stable than non-cyclic structures.

- Note that double bonds in linear structures also have delocalized ‘pi’ bonds.
**Dipole Moment**

- The overall polarity of a molecule depends on both the presence of polar bonds and on the geometry of the molecule.
- Planar, trigonal, tetrahedral
- The determinant of overall polarity is the vector sum of the individual polar bonds (i.e., dipole moment of individual bonds), which is called the molecular dipole moment.

\[
\begin{align*}
\text{H} & \quad \text{H} \\
\text{C} & \quad \text{O} \\
\text{Cl} & \quad \text{O} \\
\end{align*}
\]

\[\rho = 6.2 \times 10^{-30} \text{ Cm} \quad \text{or} \quad 1.84 \text{ D} \quad \text{(debyes)}\]

**Intermolecular Forces**

- Attraction between molecules due to instantaneous dipole moments.

**Substance** | **Molecular Mass** | **Dipole Moment** | **Boiling Point**
---|---|---|---
propane, CH₃CH₂CH₃ | 44 | 0.1 | 231
dimethyl ether, CH₂OCH₂ | 46 | 1.3 | 248
methyl chloride, CH₂Cl | 50 | 2.0 | 249
acetaldehyde, CH₂CHO | 44 | 2.7 | 264
acetonitrile, CH₂CN | 41 | 3.9 | 355
Functional Groups impart characteristics upon molecules that are important in intermolecular interactions and reactivity

- **Alkyl** (can be denoted by R)
- **Hydroxy** (alcohol, if phenol then R = \( -\text{C}_2\text{H}_4\text{OH} \))
- **Mercapto** (thiol, mercaptan)
- **Ether**
- **Sulfide** (thioether)
- **Amino** (primary amine, \( R_2 = R_3 = \text{H} \))
  - **Secondary amine**, \( R_3 = \text{H} \)
  - **Tertiary amine**, \( R_1, R_2, R_3 = \text{C} \)
  - **Aniline** if \( R = \text{-C}_2\text{H}_4\text{NH}_2 \)
- **Carbonyl** (ketone, aldehyde when \( R_2 = \text{H} \))
- **Carboxy** (carboxylic acid)
- **Ester** (carboxylic acid ester)
- **Thioester**
- **Phosphate ester** (if X = O); **Thiophosphate ester** (if X = S)
- **Nitro**
- **Nitroso**

**Saturation**

\[ \text{H}_3\text{C} \text{CH}_2 \text{CH}_3 \]

**Unsaturation**

\[ \text{H}_3\text{C} \text{CH}_2 = \text{CH}_3 \]

**Vapor Pressure**

- The pressure of the vapor of a compound at equilibrium with its pure state
  - Think of VP as the escaping tendency of the molecules of a pure substance from itself
- Compound to compound variations arise as a result of intermolecular forces
**Water Solubility**

- The amount of a substance that dissolves in a given quantity of water at a given temperature to form a saturated solution
  - Think of it as the escaping tendency of molecules from one another when placed in water

**Limitations to Water Solubility**

- Regular, highly ordered structure of water
  - Results from high degree of hydrogen bonding
  - Cause of very high surface tension for such a small molecule
  - Surface tension is the intermolecular, cohesive attraction between like molecules of a liquid that cause it to minimize its surface area
  - Causes the high boiling point of water
- A solute dissolving in water has to disrupt the orderly structure of water (with consequent energy costs)
  - Think of it as punching a hole in the water
**Highly ordered structure of water due to extensive hydrogen bonding between molecules**

http://hyperphysics.phy-astr.gsu.edu/hbase/electric/diph2o.html#c3

**Imbalance of intermolecular forces at “edge” of water tends to draw outer layer of molecules into the interior, thereby reducing the surface area.**

**The water molecules in the interior of the liquid are attracted equally in all directions.**

**Surface tension is the measure of inward forces at the surface that must be overcome to expand the surface area of the liquid.**

---

**Solutes (for ex., any contaminant in water) disrupt the water structure. That is, the intermolecular forces between water molecules are disrupted.**

**If contaminant has functional groups that can hydrogen bond with water, then the water structure is disrupted less and more of the contaminant can dissolve in the water (comparatively less free energy in the system)**

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**Facilitation & Limitations of Water Solubility**

- If a dissolving molecule has functional groups that allow hydrogen bonding, then the regularity of the water structure is disrupted less than if the molecule lacked the capability of hydrogen bonding.
- If no polar functional groups, than more energy must be expended to disrupt the water structure.
  - Thus, entropy would necessarily be higher, and consequently, WS would be less.

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**Schwarzenbach et al. 1993**
Examples of Water Solubility Ranges for Different Groups of Contaminants

Schwarzenbach et al. 1993

Distilled Water vs. Seawater

<table>
<thead>
<tr>
<th>Compound</th>
<th>Solubility, distilled H₂O (ppm)</th>
<th>Solubility, seawater (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>toluene</td>
<td>506.7 ± 6.1</td>
<td>418.5 ± 5.0</td>
</tr>
<tr>
<td>acenaphthene</td>
<td>2.42 ± 0.02</td>
<td>1.84 ± 0.04</td>
</tr>
<tr>
<td>pyrene</td>
<td>0.13 ± 0.01</td>
<td>0.09 ± 0.01</td>
</tr>
</tbody>
</table>

Effect of Temperature on Solubility

<table>
<thead>
<tr>
<th>Compound</th>
<th>Molar Volume (mL)</th>
<th>15°C log solubility (ppb)</th>
<th>20°C log solubility (ppb)</th>
<th>25°C log solubility (ppb)</th>
</tr>
</thead>
<tbody>
<tr>
<td>toluene</td>
<td>109</td>
<td>5.61</td>
<td>5.61</td>
<td>5.62</td>
</tr>
<tr>
<td>acenaphthene</td>
<td>150</td>
<td>2.33</td>
<td>2.74</td>
<td>3.26</td>
</tr>
<tr>
<td>pyrene</td>
<td>172</td>
<td>1.75</td>
<td>1.85</td>
<td>1.95</td>
</tr>
</tbody>
</table>


Other dissolved substances can affect water solubility of a compound. Solubility can be facilitated by the co-dissolved solvent re-orienting the water structure so that the compound “fits” into the water structure in a more thermodynamically favorable manner.

Recall that solution pH is the negative logarithm of the hydrogen ion [H⁺] concentration.

\[
\text{H}_2\text{O} \leftrightarrow \text{H}^+ + \text{OH}^-
\]

\[\text{H}^+ + \text{H}_2\text{O} \leftrightarrow \text{H}_3\text{O}^+\text{, and } K = 1 \text{ at equilibrium;}\]

\[K_w = [\text{H}^+] \cdot [\text{OH}^-] = 1 \times 10^{-14} \text{M (the ion product constant for water)}\]

For any acid (or base):

\[\text{HA} + \text{H}_2\text{O} \leftrightarrow \text{H}_3\text{O}^+ + \text{A}^-\]

\[K_a = \frac{[\text{H}_3\text{O}^+] [\text{A}^-]}{[\text{HA}]} \text{ acidity dissociation constant}\]

\[\text{pH} = \text{pK}_a + \log \left(\frac{[\text{A}^-]}{[\text{HA}]}\right)\]

\text{pK}_a \text{ can be thought of as a measure of the tendency of an acid to dissociate (i.e., deprotonate); by the same analogy, } \text{pK}_b \text{ is the tendency of a base to protonate.} \text{ pK}_a \text{ and } \text{pK}_b \text{ can be thought of as the tendency of an acid to dissociate or a bases to accept a proton (H⁺). When } \text{pH} = \text{pK}_a, \text{ the concentration of A⁻ (the salt form) and HA are equal.}\]
Note that proton dissociation would only occur at unrealistically high pHs.

**Molar Volume**

- The volume occupied by one mole of a substance in the gas phase.
- Regarding liquids and solids, the molar volume is the volume occupied by a mole of substance in aqueous solution.
- In a very dilute solution, the molar volume approaches that of water (18 x 10^{-6} m^3/mol)
- Correlated with WS and VP

As molar volume increases, the entropy for dissolution also increases because more energy has to be put into the system to reorganize the water.

**Schwarzenbach et al. 1993**

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