Weaving Toxicology Principles into a Senior Level Green Chemistry Lecture Course

Jane E. Wissinger
Department of Chemistry
University of Minnesota

21st Green Chemistry & Engineering Conference
Reston, VA
Tuesday, June 13, 2017
10:50-11:10am

University of Minnesota
Green Chemistry Lecture Course
Department of Chemistry

- Junior/Senior – 4601 (class size 30-45)
- Elective
- Majority chemistry/chemical engineering majors
- Other/minors – food science, water science, physiology, art
- Survey Course- 2-3 lectures per topic
Format/Content


- **Readings:** 2-3 literature articles and/or videos (flipped) before class

- **Class time** – Some lecture but mostly assignments, projects and presentations
  – Active learning classrooms
Content/Format

- **Flipped Content (videos created)**
  - Lee Penn – Green Nanotechnology
  - Bill Tolman – Catalysis
  - Jane Wissinger – Greener Solvents (Alternative Rx Media)
  - Toxicology – Heiko Schoenfuss (St. Cloud)
  - Policy – Steve Kelley

- **Guest Speakers**
  - 3M, Sustainable Plastics, NatureWorks, Cargill, Dr. Nancy Carpenter (Morris), etc..

- **Green Metrics**
Grade

- In-class quizzes (15.0%)
- Green Chemistry Minute Presentation (12.5%)
- Attending a seminar/webinar of choose (5.0%)
- Homework/in-class assignments & participation (12.5%)
- Term Paper (35%)
- Final Examination (20%)
- >50 % Tailored to student choice/interest of topic
Pre-Survey

What background and or experiences do you have already in Green Chemistry and/or Sustainability studies?

Courses:

- Organic Chemistry Laboratory: A Green Approach
- Bioproducts and Biosystems Eng Classes
- Sustainable Housing – Community, Environment and Technology & “Tiny House”
- Biorenewable Resources
- TA – Environmental Biology (included toxicology)

Internships:

- Industrial internship looking for BPA replacement
- Sustainability of Food Systems
- Science and Politics of Global Warming
- Internships in Biofuels, Environmentally Friendly Products, Biodegradable Microbeads
Pre-Survey

Are there particular areas of focus (e.g. organic reactions, toxicology, industry use of green chemistry, etc..) you hope to learn?

• 30% specifically identified toxicology as high area of interest

• One Student’s response:

After you mentioned toxicology in class, it reminded me of a trivia question involving toxicity that I didn't know the answer to. This actually disturbed me at the time because I felt as a chemist that I should know which chemicals are more toxic, so I can either avoid using them, or use extra care.
Progression of Toxicology Topics

• Risk Defined

Risk = \( f(\text{exposure, hazard}) \)

Discuss different scenarios and problems with each:
Reduce exposure with PPE
“dilution is the solution to pollution”
etc.

Green Chemistry approach is to reduce/eliminate the hazard
One of First Homework Assignments..

- Toxic Release Inventory (TRI)
  
  - [https://www.epa.gov/toxics-release-inventory-tri-prog](https://www.epa.gov/toxics-release-inventory-tri-prog)
  
  - Find the toxic chemical releases for your city
  - What is the total amount of releases this year?
  - What is the single largest chemical by weight released?
  - What industry/company released the most waste?
  - Write a short summary of the toxic endpoints.

  - **Highlights what chemicals are on the list**
Unit: Assessing/Design for Reduced Hazard

Reading Assignments


(1) Literature Paper Discussion

• What were the goals of authors?
• “Lipinski-like rules” for toxicity

Terms/concepts to know

• *In-silico* (in *vivo*, in *vitro*)
• TRI
• Lipinski’s “Rule of Five”
• Globularity
• Log $P_{oct/water}$ or $P_{o/w}$
• Four modes of entry to organism

---

MoDRN Module: Physiochemical Properties

• **Module 1: Aqueous and Lipid Solubility**
  Pre-Class: read and prepare for class activities
  – Introduction
  – “Green Chemistry Molecular Design Pyramid” video
  – EPA ExpoBox assignment
    • Fate and Transport
    • Physiochemical/Environmental Factors

  – **Assignment** – *Relationship of Molecular Structure to Hydrophobicity & K_{ow} (Chlorinated Benzenes & PCB)*

http://modrn.yale.edu/education/undergraduate-curriculum/modrn-u-modules/principles-toxicology-modules
MoDRN Module: Physiochemical Properties Modules

• In-class
  – Reviewed major concepts
  – Reviewed answers to the assignment


  – Students designed their own series of compounds to study comparing Log P and structural
  – Presented results to the class, identifying if a trend was observed
MoDRN Modules: Physiochemical Properties

• **Module 2: Redox Reactions**
  Pre-class Assignment:
  Read and watch video
  Added Redox review handouts

• **In-class -**
  – Lecture and discussion - balance needed in cells, Cytochrome P450 and relationship to mechanisms of toxicity
  • Benzene, PAH
MoDRN Modules: Principles of Toxicology

• **Module 3: ADME and Toxicology**
  – Absorbed, Distributed, Metabolized, Eliminated
  – Read and watch the video for each module. Take notes. In class we will discuss and work through the assignments.

  – Students applied these concepts in all subsequent assignments
    • Examples: “Dyeing to be Green” homework assessing dye ADME
    • Their own term papers
Match

Physicochemical Property

- Molecular Size
- REDOX Potential
- Solubility
- LogP/pKA

ADME Component

- Absorption
- Distribution
- Metabolism
- Excretion

http://modrn.yale.edu/education/undergraduate-curriculum/modrn-u-modules/principles-toxicology-modules
Guest Toxicologist

Dr. Heiko L. Schoenfuss
- St. Cloud State University
- Director - The Aquatic Toxicology Laboratory
  “investigates the costs of contaminants of emerging concern on aquatic life…”

- 6 Videos assigned to students (and readings) – 1 guest lecture, 2 discussion days (me)

http://web.stcloudstate.edu/aquatictox/people1.html
Paradigm of “dose makes the poison” not always true
2. Key Concepts

*Not a unified science* (mechanistic, descriptive, clinical, environmental, regulatory)

*Exposure Concepts*
3. Complications – would not directly predict

DDT

Diethylstilbestrol (DES)
4. Endocrine Disruptors

As contaminants of emerging concern (CEC)

Human Excretion concentrated in wastewater treatment – measurements in MN
Toxicology Videos

5. Case Study
How an environmental toxicologist assesses environmental impact
Subsequent Use of Tox Principles

- Catalysts – metals
- Nanotechnology – size and transport
  - TiO$_2$, nanotubes
- Dyeing to be Green
- Term Papers
Summary

• Principles of Toxicology were introduced early in a green chemistry course through:
  – TRI study
  – MoDRN modules ($K_{ow}$, ADME, assignments)
  – Guest Environmental Toxicologist

• Students demonstrated the ability to apply these concepts to new topics later in the semester and in their own term paper and assignments

THANK YOU!
Lipinski rule of five

The medicinal chemist Christopher Lipinski and his colleagues analysed the physico-chemical properties of more than 2,000 drugs and candidate drugs in clinical trials, and concluded that a compound is more likely to be membrane permeable and easily absorbed by the body if it matches the following criteria:

- Its molecular weight is less than 500.
- The compound's lipophilicity, expressed as a quantity known as logP (the logarithm of the partition coefficient between 1-octanol and water), is less than 5.
- The number of groups in the molecule that can donate hydrogen atoms to hydrogen bonds (usually the sum of hydroxyl and amine groups in a drug molecule) is less than 5.
- The number of groups that can accept hydrogen atoms to form hydrogen bonds (estimated by the sum of oxygen and nitrogen atoms) is less than 10.

http://www.nature.com/nature/journal/v481/n7382/box/481455a_BX1.html
<table>
<thead>
<tr>
<th>Monday</th>
<th>Tuesday</th>
<th>Wednesday</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/16</td>
<td></td>
<td>1/18</td>
</tr>
<tr>
<td>Holiday (MLK)</td>
<td></td>
<td>History of Chemistry, the Environmental Movement and Green Chemistry</td>
</tr>
<tr>
<td>1/23</td>
<td></td>
<td>1/25</td>
</tr>
<tr>
<td>History Continued, Science and Politics, where Green Chemistry fits in. Risk defined.</td>
<td></td>
<td>The 12 Principles of Green Chemistry and Green Engineering Principles Overview TRI Success</td>
</tr>
<tr>
<td>A &amp; W, Chapter 1,2</td>
<td></td>
<td>A &amp; W, Chapter 3,4</td>
</tr>
<tr>
<td>1/30</td>
<td></td>
<td>2/1</td>
</tr>
<tr>
<td>Green Metrics: Atom Economy, Reaction Efficiency – Classification of reactions</td>
<td></td>
<td>Green Metrics: E-factor and Product Mass Intensity (Pharma)</td>
</tr>
<tr>
<td>A &amp; W, Chapter 7 Nicole &amp; John (GM)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2/6</td>
<td></td>
<td>2/8</td>
</tr>
<tr>
<td>Greening Organic Reactions through Alternative Reaction Media</td>
<td></td>
<td>Greening Organic Reactions through Alternative Reaction Media</td>
</tr>
<tr>
<td>Watch Wissinger videos – Greener Solvents</td>
<td></td>
<td>Eric &amp; Sam (GM)</td>
</tr>
<tr>
<td>A &amp; W, Chapter 9.4.1-4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2/13</td>
<td></td>
<td>2/15</td>
</tr>
<tr>
<td>Poster Presentations of Alternative Reaction Media</td>
<td></td>
<td>Assessing Hazard and Molecular Design for Reduced Hazard – introduction Toxicity of “Bad actors” MoDRN</td>
</tr>
<tr>
<td>Tentative Title and 1 paragraph summary for term paper due 2:30 p.m.</td>
<td></td>
<td>Chance &amp; Jake (GM)</td>
</tr>
</tbody>
</table>
### February/March, Spring 2017

<table>
<thead>
<tr>
<th>Monday</th>
<th>Tuesday</th>
<th>Wednesday</th>
</tr>
</thead>
<tbody>
<tr>
<td>2/20</td>
<td></td>
<td>2/22</td>
</tr>
<tr>
<td>Toxicology – Heiko Schoenfuss</td>
<td>Toxicology continued</td>
<td>Toxicology continued</td>
</tr>
<tr>
<td>Watch Videos</td>
<td>A&amp; W, Chapter 5, 8</td>
<td>A&amp; W, Chapter 5, 8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Kaitlin &amp; Ryan (GM)</td>
</tr>
<tr>
<td>2/27</td>
<td>3/1</td>
<td>3/8</td>
</tr>
<tr>
<td>Jared &amp; Liz (GM)</td>
<td>A&amp; W, Chapter 9.1.3</td>
<td>Life Cycle of PET bottles (fossil vs. bio-based) – Luyi Chen</td>
</tr>
<tr>
<td>3/6</td>
<td>3/10</td>
<td>3/10</td>
</tr>
<tr>
<td>Platform Chemicals from Biomass</td>
<td>Draft 1 of term paper (5:00 p.m.) due</td>
<td>Draft 1 of term paper (5:00 p.m.) due</td>
</tr>
<tr>
<td>Ali &amp; Josh (GM)</td>
<td></td>
<td>Life Cycle of PET bottles (fossil vs. bio-based) – Luyi Chen</td>
</tr>
<tr>
<td>3/13</td>
<td>3/15</td>
<td>Spring Break</td>
</tr>
<tr>
<td>Spring Break</td>
<td></td>
<td>Spring Break</td>
</tr>
<tr>
<td>3/20</td>
<td>3/22</td>
<td>3/29</td>
</tr>
<tr>
<td>Sustainable Plastics – renewable/degradable</td>
<td>Catalysis – Professor Tolman</td>
<td>Sustainable Plastics - Design for Degradation</td>
</tr>
<tr>
<td>A&amp; W, Chapter 6</td>
<td>Watch Tolman Videos</td>
<td></td>
</tr>
<tr>
<td>Matt &amp; Riley (GM)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3/27</td>
<td>3/29</td>
<td>Spring Break</td>
</tr>
<tr>
<td>Catalysis – Professor Tolman</td>
<td></td>
<td>Spring Break</td>
</tr>
<tr>
<td>A&amp; W, Chapter 4.9, 9.4.1, 9.4.2.2 etc.</td>
<td></td>
<td>Spring Break</td>
</tr>
<tr>
<td>Kayla &amp; Aimee (GM)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3/27</td>
<td></td>
<td>Spring Break</td>
</tr>
<tr>
<td>Catalysis – Professor Tolman</td>
<td></td>
<td>Spring Break</td>
</tr>
<tr>
<td>A&amp; W, Chapter 4.9, 9.4.1, 9.4.2.2 etc.</td>
<td></td>
<td>Spring Break</td>
</tr>
<tr>
<td>Kayla &amp; Aimee (GM)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### April/May, Spring 2017

<table>
<thead>
<tr>
<th>Monday</th>
<th>Tuesday</th>
<th>Wednesday</th>
</tr>
</thead>
<tbody>
<tr>
<td>4/3</td>
<td>4/5</td>
<td>4/5</td>
</tr>
<tr>
<td>Cargill – Solution based approach – Brent Aufdembrink</td>
<td>Choice of Topic – Obesogens, brominated flame retardants, endocrine disruptors</td>
<td>Tyler &amp; Sharmaarke (GM)</td>
</tr>
<tr>
<td>Peer review assignments given</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4/10</td>
<td>4/12</td>
<td>4/19</td>
</tr>
<tr>
<td>Green Nanotechnology – Professor Penn</td>
<td>Nanotechnology, continued</td>
<td>Steve Kelly – Chemistry Policy – a case study</td>
</tr>
<tr>
<td>4/14 – Peer reviews due (2:30 p.m.)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4/17</td>
<td>4/19</td>
<td>4/26</td>
</tr>
<tr>
<td>Renewable Energy – the case for solar cells &amp; wind - Nancy Carpenter</td>
<td>Dyeing to be Green</td>
<td>Dyeing to be Green</td>
</tr>
<tr>
<td>David &amp; Ravyn (GM)</td>
<td></td>
<td>Claire &amp; Terry (GM)</td>
</tr>
<tr>
<td>4/24</td>
<td>5/3</td>
<td>5/9</td>
</tr>
<tr>
<td>Dyeing to be Green</td>
<td>Semester in Review</td>
<td>4601 Final – Room TBD</td>
</tr>
<tr>
<td>Akshay &amp; Daniel (GM)</td>
<td></td>
<td>8:00-10:00 a.m.</td>
</tr>
<tr>
<td>5/1</td>
<td>5/3</td>
<td></td>
</tr>
<tr>
<td>Green Chemistry Successes Green Chemistry Presidential Awards – presentations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Final Term Paper due 8:00 a.m.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A &amp; W, Chapter 9</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>