Integrative Physiology used for Toxicology

Dr. Joseph Covi
(Integrative Physiologist)

Past teaching and research experience at…

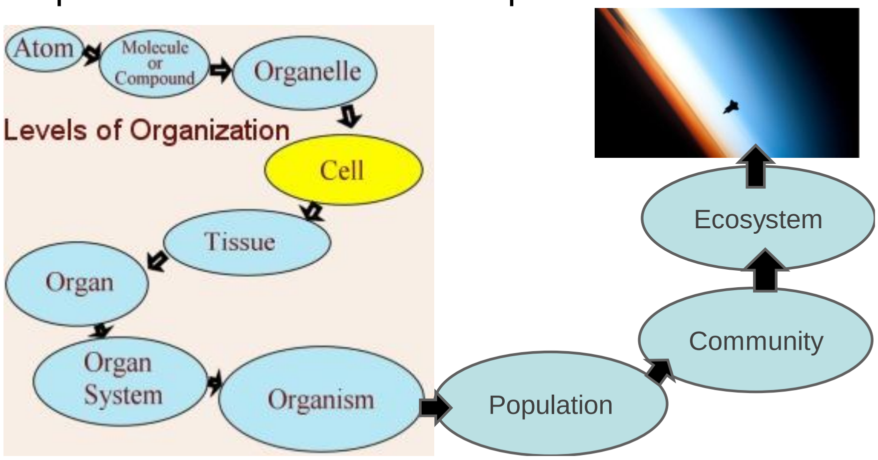
- Colorado State University
- University of Colorado at Boulder
- University of California at Davis
- Louisiana State University
- University of Wisconsin, Stevens Point

What scientific discipline is right for you?

1. **Ecology… the study of how life forms interact with each other and the physical environment.**
2. **Anatomy… the study of structure.**
3. **Physiology… the study of function.**
4. **Toxicology… the study of how chemicals adversely affect living things (toxicology is a sub-discipline of physiology.)**
5. **Biochemistry… the study of how molecules interact in living systems.**
6. **Molecular Biology… the study of how genes are passed on and expressed.**
7. **Evolutionary Biology… the study of how life forms came to be ("unity and diversity").**

Specialist vs. Integrative Biologist

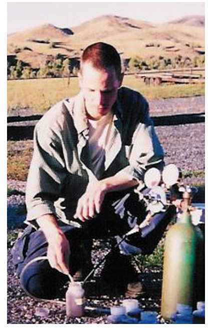
1. Specialists generally focus on 3 levels or less
2. Integrative Biologists look at whatever level will help them answer a scientific question.



What do students do in my lab?

1. **Ask and answer important questions.**
2. **Integrative and comparative physiological research—a very inclusive sub-discipline of physiology that uses:**
   a. **Ecology (how environment influences physiology)**
   b. **Evolutionary Biology (compare species traits)**
   c. **Anatomy (how environment influences structure)**
   d. **Biochemistry (how chemicals alter signaling)**
   e. **Molecular Biology (how chemicals alter gene expr.)**
3. **In a nut shell, my students study how environmental toxins influence structure and function during growth and development.**

All good science begins with curiosity.



Scientific Method:

1. Make an observation… **that brings up a question because you are curious**.
2. Build a Model to better understand what we know already!
3. Propose a hypothesis to explain the observation.
4. Design an experiment to test the hypothesis.
5. Analyze data and make a new model with it.

Observation… zooplankton embryos must see a lot of environmental insults before they develop.

Diaptomus sanguineus

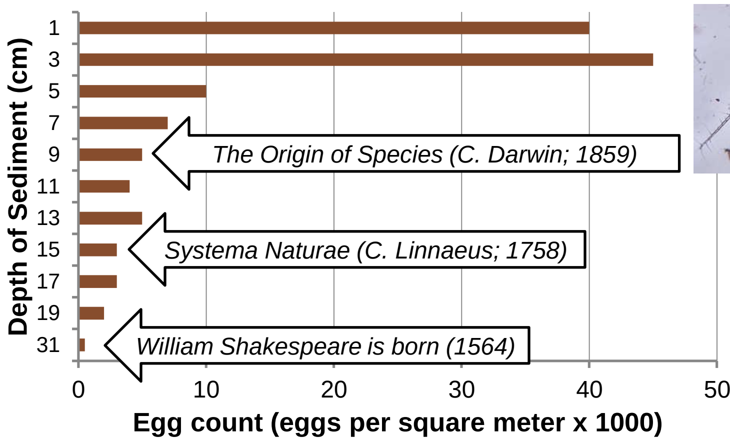


Figure adapted from Hairston and Kearns (2002) Temporal dispersal: ecological and evolutionary aspects of zooplankton egg banks and the role of sediment mixing. Integ. and Comp. Biol. 42: 481-491.

Poster child for the accumulation of POPs (Persistent Organic Pollutants)

Levels of PCBs:

1.3 mg/Kg = disruption threshold

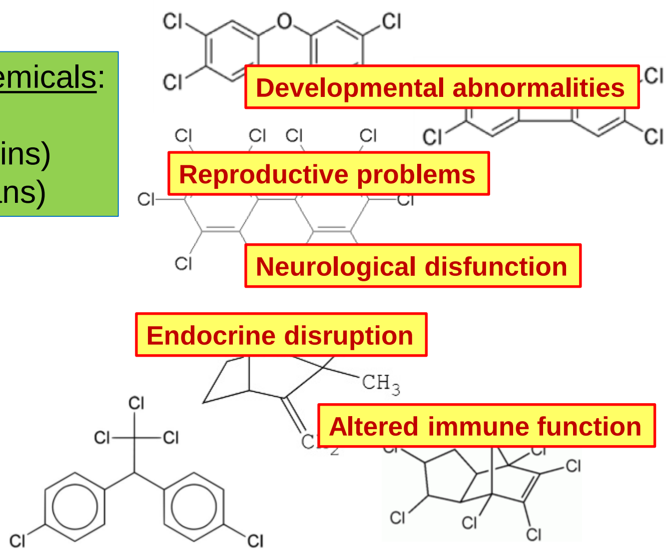
>20 mg/Kg found in some whales

Examples of POPs:
PCBs (polychlorinated biphenyls)
PCDDs (polychlorinated dibenzo-p-dioxins)
PCDFs (polychlorinated dibenzofurans)

Persistent Organic Pollutants (POPs)

1. Industrial chemicals:
   PCBs
   PCDDs (dioxins)
   PCDFs. (furans)

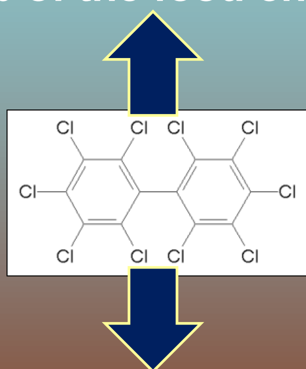
2. Pesticides:
   Toxaphene
   Chlordane
   DDT
   Mirex



One of Dr. Covi's NEW questions: Are zooplankton species that rely on prolonged dormancy more susceptible to impacts from toxicants than species that don't rely on dormancy for success?

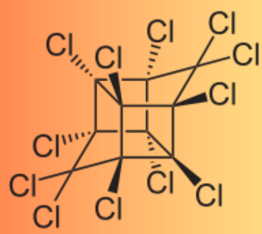
Where do POPs accumulate in ecosystems? (model building)

Top of the food chain



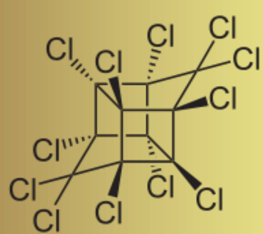
Settled organic matter (sediment in aquatic systems)

Where do POPs accumulate in vertebrates? (model building)

Brain, Muscle, Blood, etc. ←  → **Adipose & Liver**

POPs are generally lipophilic ("fat loving")

Could POPs accumulate in zooplankton? (Model building)

Membranes, Mitos, Golgi, etc. ←  → **Lipid granules**

Yes, because…
POPs are generally lipophilic ("fat loving")

Where do we look for zooplankton embryos? (Model building)

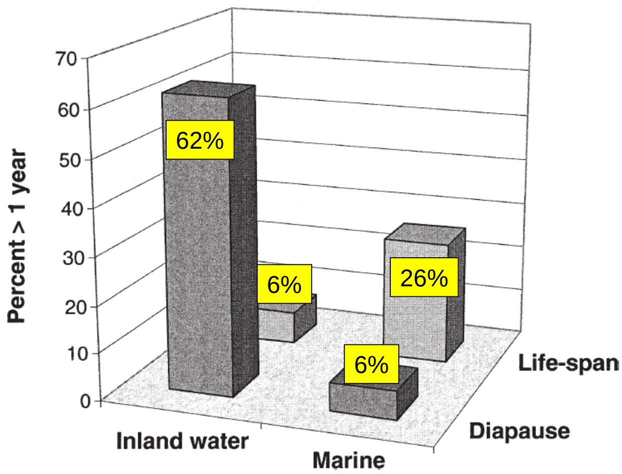


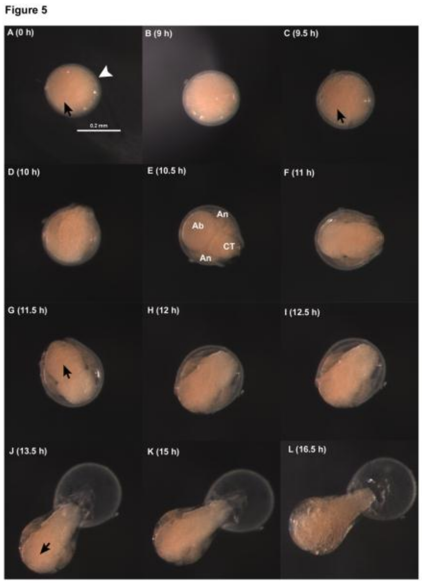
FIG. 1. Distribution of prolonged life span (>1 yr) in crustaceans, either as diapausing eggs or as iteroparous adults, for species living in inland waters and marine habitats. Data from Hairston and Cáceres (1996).

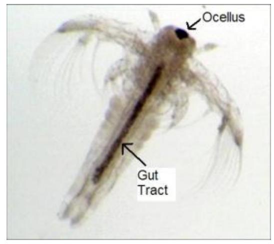
Poster **children** for the accumulation of POPs (Persistent Organic Pollutants)

Verified to live >40 years in captivity, estimated to have similar lifespan to human in the wild.

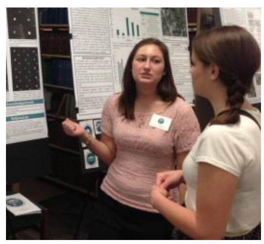
Adults may only live for a few months, but the embryos live for years to centuries in anoxic sediment.

Jamie Gerlach's Research





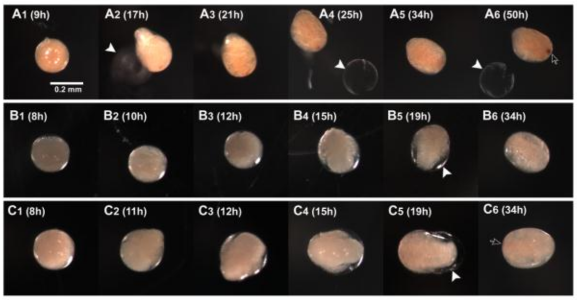
Kristin Ruggiero's Research (Jamie's Analysis)

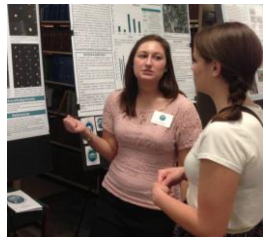


Development (embryo → larva)

Kristin Ruggiero's Research (Jamie's Analysis)

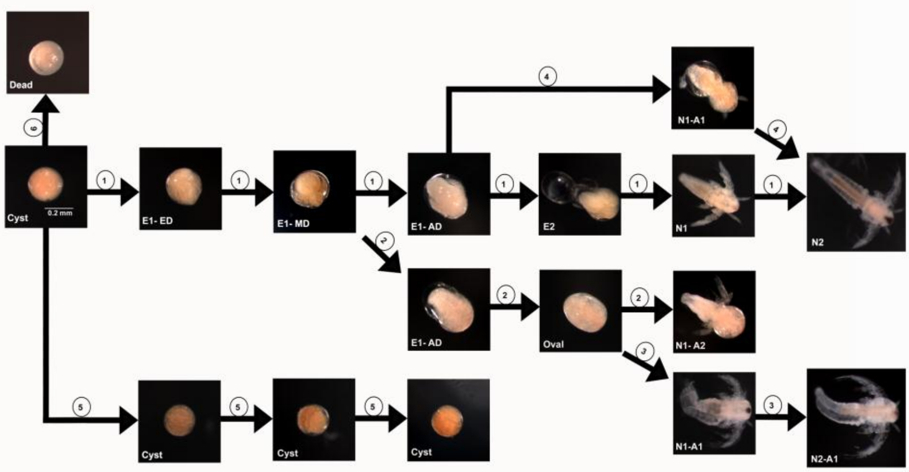
Figure 7





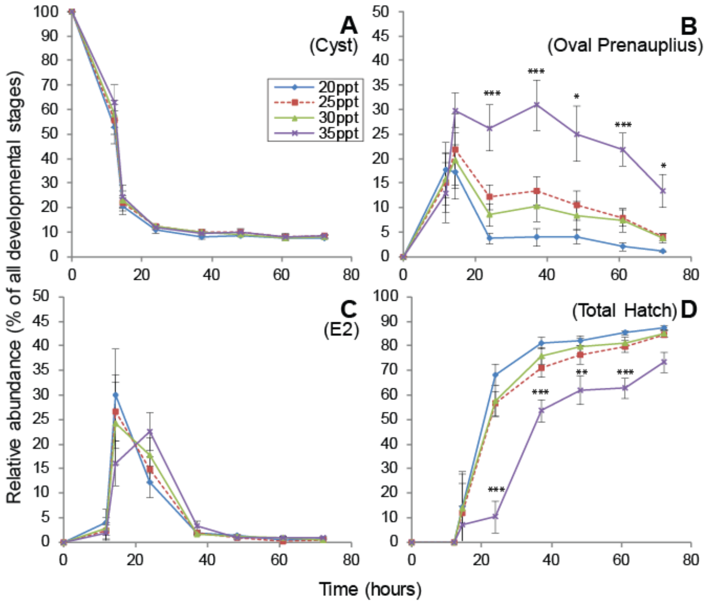
Development (embryo → abnormal pre-larva)

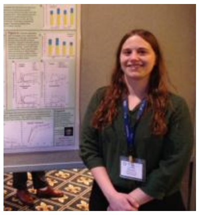
Jamie Gerlach's Research



Development (0 h → 24-36 h)

Courtney Neumeyer's Research





Who I've worked with so far:

- **Mentored Students (Graduated)**
  1. Jamie Gerlach
  2. Kristen Ruggiero
  3. Evan Hutchison
  4. Matt Gunderson
  5. Kevin Carlson
  6. Alyse Milanowski
  7. Jeremiah Snortum
  8. Alexandra Anderson
  9. Travis Rusch
  10. Elise Boehm
  11. Emily Knoll
  12. Ashley Larson
  13. Lisa Axtman
  14. Drew Iman
  15. Katie Regelson
  16. Stacie Amburgey
  17. Il-Gyu Cho
  18. Linsey Atchinson
  19. Peter Exener
  20. Sere Williams
  21. Lindsay Martin
  22. Lindsay Brier
  23. Kristin Van Ort
  24. Brandon Bader
  25. Casey Ehlinger
  26. Jocelyn Riehl
  27. Keith Dmytrow
  28. Lindsey Progen
  29. Rosemary Townsend
  30. Andrea Gomez
  31. Jodi Hoppes
  32. Samantha Roth
  33. Ali Abuhagr
  34. Kathy Cosenza
  35. Matt Stratton
  36. Jen Gunderson
  37. Audrey McDonald
  38. Stephanie Hjelmfelt
  39. Erica Chao
  40. April Flack
  41. Tyler Zarubin
  42. Sung Gu Lee
  43. Natalie Wasmundt

- **Collaborators**
  - Dirk Weihrauch
  - David Towle
  - Paul Linser
  - Markus Huss
  - Helmut Wieczorek
  - Hector Horta
  - Ernie Chang
  - Brad Marden
  - Don Mykles
  - Steve Hand
  - Brian Eads
  - Leslie Lohmiller
  - D. Ortiz-Barrientos
  - Dale Treleaven

Overview of Research Opportunities

Project 1 - Environmental

a. Examine local aquatic environments for POPs.
(Create list of POPs that might affect zooplankton.)

b. Collect sediment samples and test for “banked” embryos and toxins.

Project 2 - Organismal

a. Use multiple species (commercial and local collection) to assess variation in susceptibility to chemicals.

b. Expose whole animals to environmentally relevant toxins.

Project 3 - Subcellular

a. Grind up embryos and identify toxin accumulation site(s).

b. Determine effect of toxins on isolated organelles.

Project 4 - Molecular

a. Determine effect of toxins on gene expression.