



ES/RP 531

Fundamentals of
Environmental Toxicology

Lecture 1

History; Overview of Concepts



Instructor

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 - 509-372-7365
 - 25 years studying environmental chemistry & toxicology
 - Soils & water issues
 - Insect toxicology
 - Remediation of pesticide waste
 - Agricultural Biotechnology



PNW Minor Crop Tour
August 2003

Spray Drift Research for Enhancing IPM & Environmental Stewardship

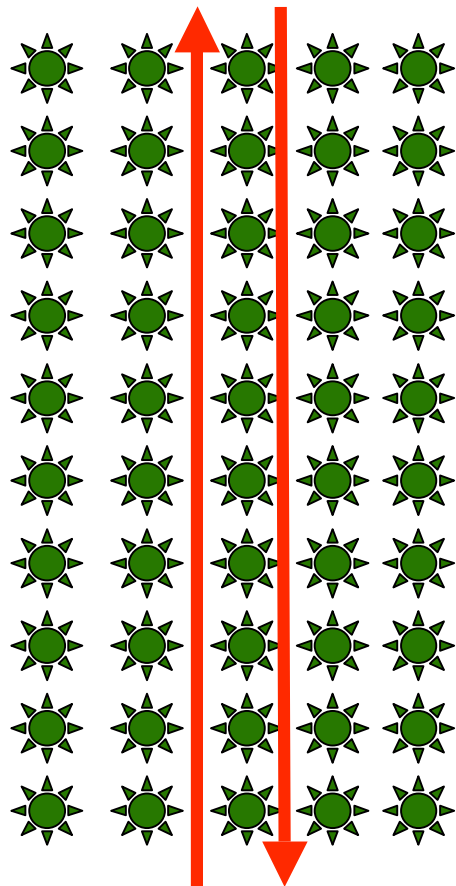


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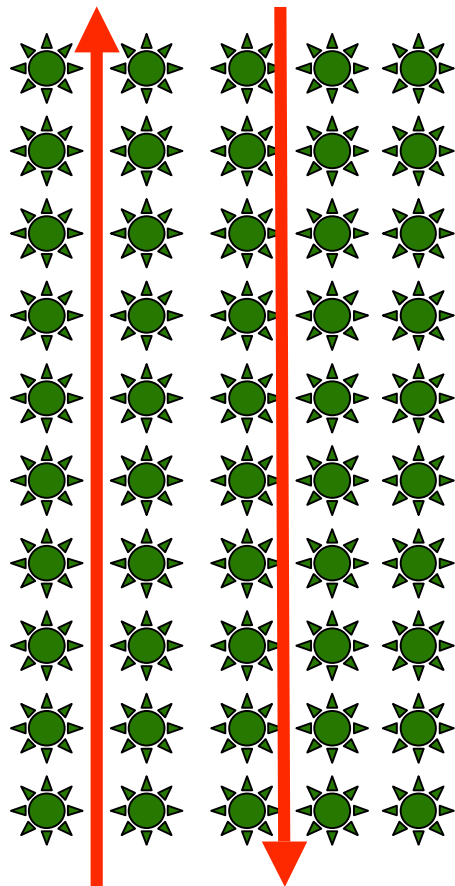
Sprayer Technology Project

- Research projects funded by the WA Tree Fruit & Research Commission
 - Use of alternative sprayer technology to reduce application rates, worker exposure, and drift
 - Development of buffer zones at the ag/urban interface, protection of water quality, and validation of AgDrift for orchards

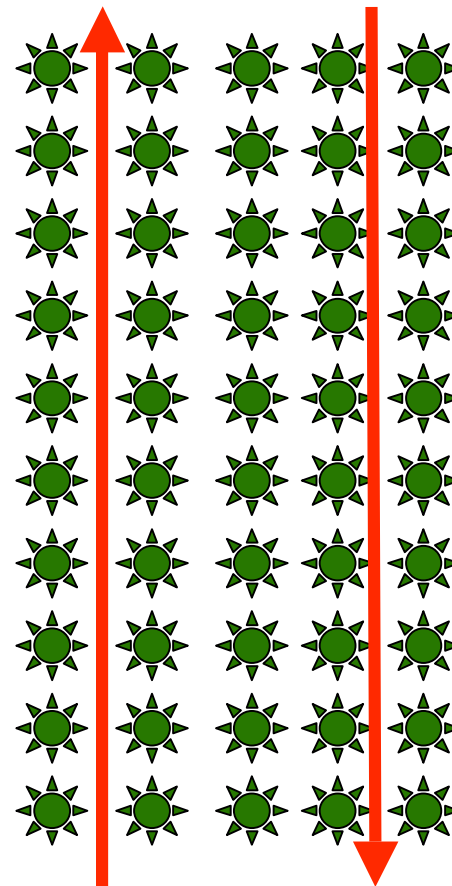




Every Row



Every Other Row



Skip Row



AB3-Row 14 North



AB3-Row 14 South



AB3-Row 15 North



ES/RP 531 -- Course Content

- Will study fundamentals of environmental toxicology in the context of the risk assessment paradigm
 - Hazard ID
 - Dose-Response
 - Exposure Assessment
 - Risk Characterization



Course Content

- For example, we will examine the endocrine disrupter hypotheses and potential effects at higher levels of organization, but the discussion will be considered as hazard identification within the context of risk assessment
- We will examine how interactions of chemicals with environment influences bioavailability and exposure, but the discussion will be considered as exposure assessment within the context of risk assessment



Course Content

- Focus will be on basic concepts, using specific invertebrate and vertebrate models (will avoid rat toxicology wherever possible)
- Focus will not be chemical specific, but will use specific chemicals to illustrate fundamental knowledge of toxicology hazards



FYI: ES/RP 532;

Applied Environmental Toxicology

- Offered fall 2004
- Focus on specific groups of contaminants examining issues from A to Z
 - Manufacture & Release
 - Physicochemical Properties
 - Environmental Chemistry
 - Toxicology (mammalian & environmental)
 - Epidemiology



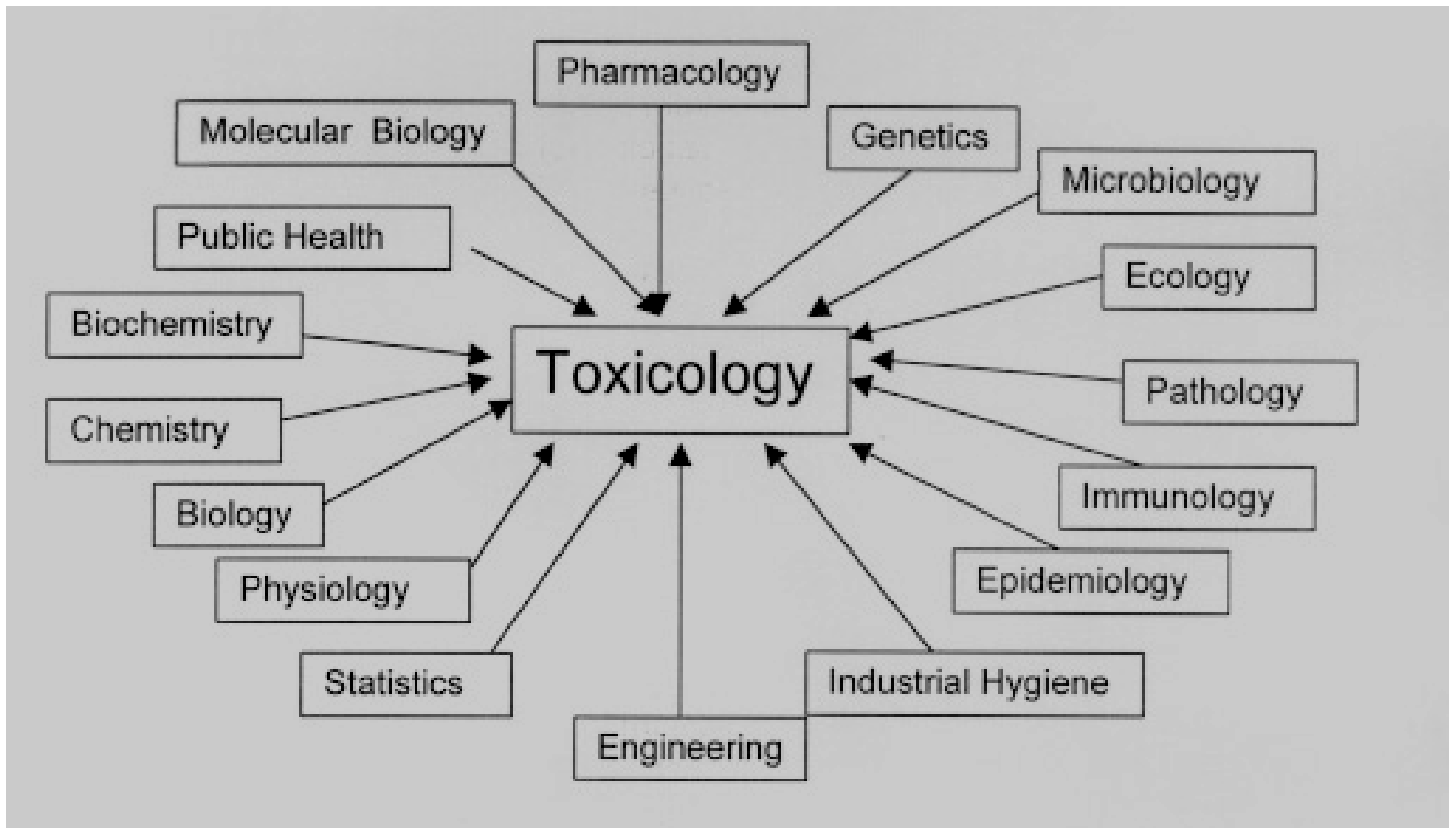
Evaluation

- Three take-home evaluations, each worth 25% of grade
 - Due the following class
- Risk Assessment “Essay”
 - You choose the chemical and go to town, deconstructing its risk of adverse effects using the risk assessment paradigm
 - 25% of grade; due during finals week
 - Time during several class periods to do the requisite library research



Toxicology

- “Science of poisons”
 - Too simplistic
- Evolved from a diversity of fields and encompasses a diversity of academic disciplines today (multidisciplinary)
 - Common thread
 - Chemicals, exposure, adverse effects
- Goal:
 - Prediction of human/environmental health effects



From Landis & Yu 1999

Introduction to Environmental Toxicology



Toxicology

- “..a study of the interaction between chemicals and biological systems in order to quantitatively determine the potential for chemical(s) to produce injury which results in adverse effects in living organisms, and to investigate the nature, incidence, mechanism of production, factors influencing their development, and reversibility of such effects.”
(Ballantyne et al. 1999)



Expansion of Toxicology

- Exponential increase in the number of synthetically produced industrial chemicals
- Major increase in the number and nature of new drugs, pharmaceutical preparations, tissue-implantable materials, & devices
- Increase in number & types of pesticides and other substances used in ag & food industry
- Mandatory testing and regulation
- Enhanced public awareness of potential effects
- Litigation



Key Issues in Toxicology

- Potential to cause injury predicated on close contact with tissue or organism
- Observed toxicity related quantitatively to degree of exposure
 - Dose-response relationships are of prime importance in confirming causal relationship between exposure and effect
 - Dose-response relationship important for assessing relevance of observed toxicity to practical exposure conditions
 - Dose-response relationships allow hazard evaluations & risk assessment



Toxicology = Many Subspecialties of Study

- Clinical
- Veterinary
- Forensic
- Occupational
- Pharmacological
- Toxinology
- Regulatory
- Laboratory
- Environmental



Environmental Toxicology

- Assesses the effects of contaminants, usually at low concentrations, released from commercial and domestic sites into the immediate environment and subsequently widely distributed by and in air, water, and soil
 - Uses disciplines of study common among all toxicology subspecialties



Environmental Toxicology vs. Toxicology

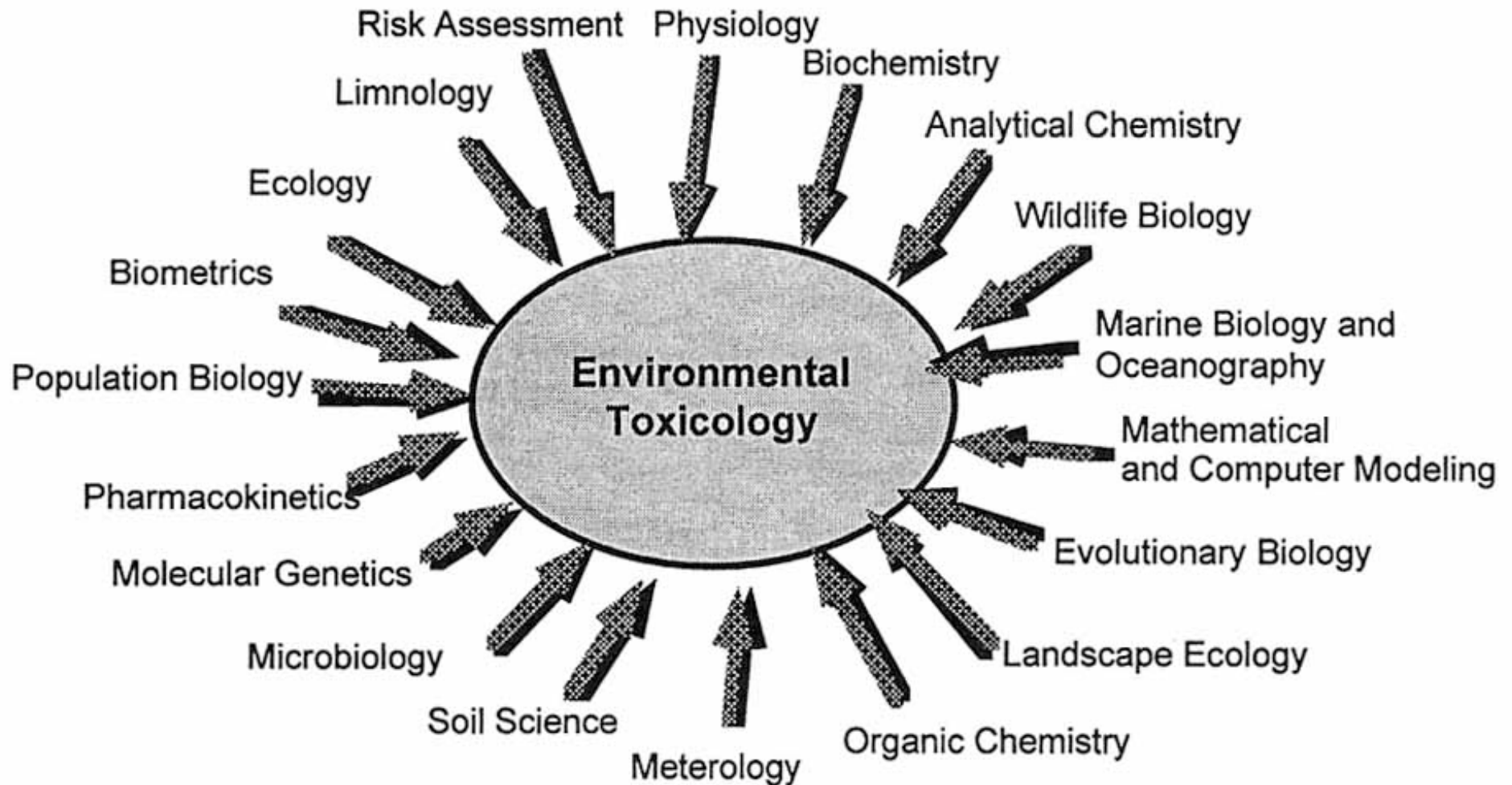
- Toxicology is usually mammalian oriented with extrapolations to humans, whereas environmental toxicology is focused on environmental effects
 - Environmental effects encompasses all biota in all environments
- Toxicology concerned with effects on individual
 - Environmental toxicology has an objective of focusing on increasing higher levels of organization
 - Individual-->Population-->Community-->Ecosystem



Toxicological Tools

- Chemistry (analytical, organic, bio)
 - Biochemical toxicology
 - Pharmacokinetics/pharmacodynamics
 - Molecular/Cellular reactions
 - Mode of Action
- Ecology
 - Ecotoxicology
 - Effects at higher levels of organization

Toxicological Tools



From Landis & Yu 1999

Introduction to Environmental Toxicology



Historical Roots

- Prehistoric culture familiar with toxic effects of animal venoms and poisonous plants
- Ebers papyrus (1500 BC)
 - Egyptian document with recipes containing recognized poisons
- Greek/Roman Culture
 - Many references to poisonous plants and antidotes



Historical Roots

- Middle Ages
 - Poisoning as a political weapon
 - Rudiments of experimental toxicology practiced by Catherine de Medici in France
 - Use direct poor and sick as guinea pigs to derive the most effective poisons
 - Noted rapidity of response (“onset of action”)
 - Noted the effectiveness of a compound (“potency”)
 - Noted the degree of response in specific body parts (“specificity”; “site of action”)
 - Noted the complaints of the victim (“clinical signs & symptoms”)



Historical Roots

- Paracelsus (1494 - 1541); recognized creator of scientific discipline of toxicology; three important concepts:
 - The toxicon or toxic agent is a chemical entity
 - Modern QSAR studies
 - Response to a substance is related to dose
 - Experimentation essential
 - Distinguish between therapeutic and toxic properties
 - Distinguishable only by dose
 - Specificity of chemicals and therapeutic or toxic effects
 - Toxicology covers a wide area
 - Paracelsus interest extended from detection or accidental or intentional poisonings through environmental factors affecting populations and occupational diseases



Historical Roots

- Mattheiu Joseph Bonaventura Orfila (1787 - 1853); father of modern toxicology
 - First systematic correlation between chemical and biological information of known poisons
 - Studied effects in thousands of dogs
 - Viewed toxicology as a distinct discipline
 - “Traite Des Poisons, ou Toxicologie Generale”
 - Pointed to the necessity of chemical analysis for legal proof of lethal intoxication and devised methods for detection of poisons
 - Developed the analytical approach that has become the basis of forensic toxicology



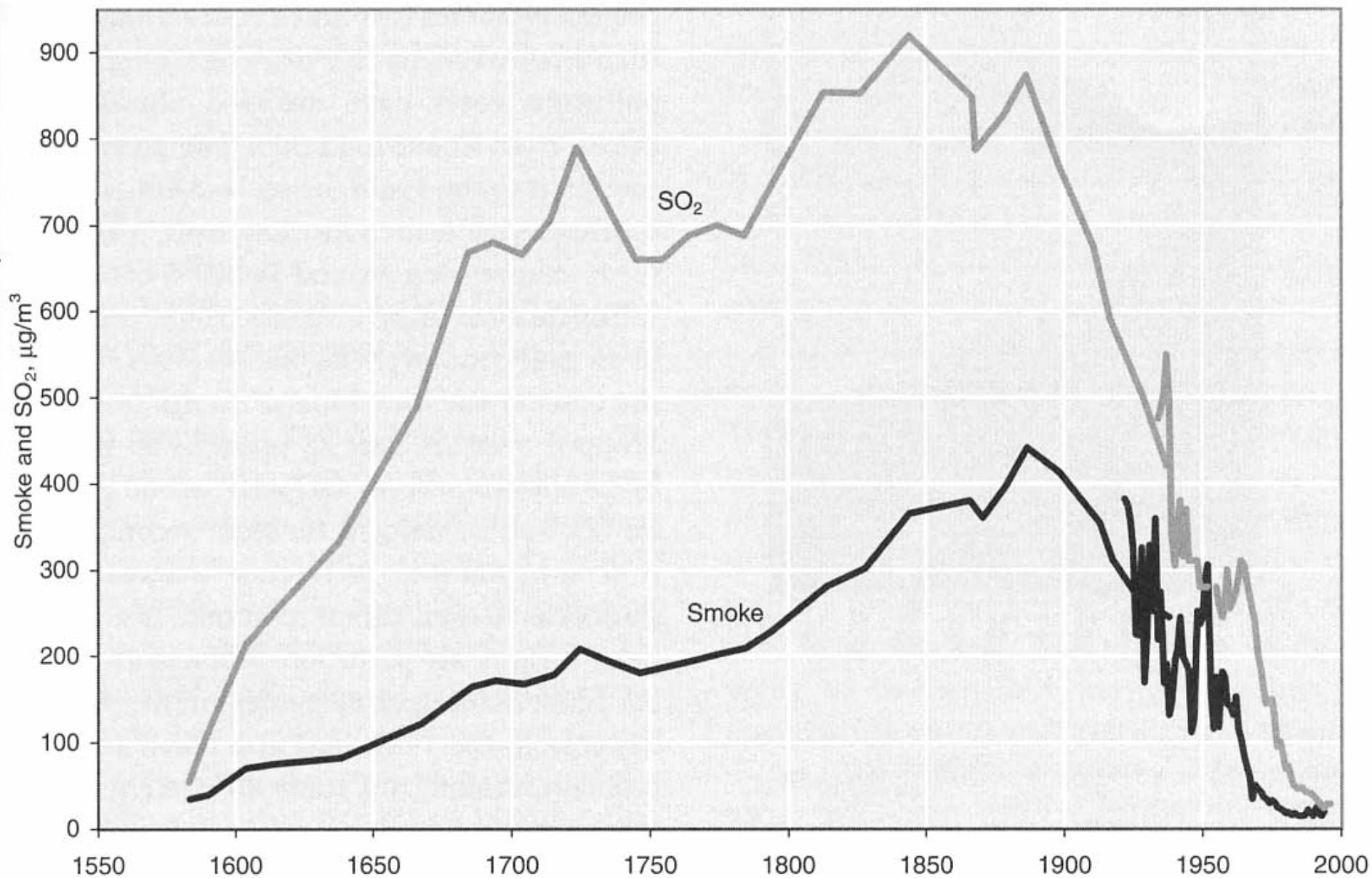
Historical Roots

- Claude Bernard (1813 - 1878)
 - Studied mechanisms of action of curare (one of several arrow poisons used by natives)
 - Recognized that “the physiological analysis of organic systems...can be done with the aid of toxic agents”



Roots of Environmental Tox.

- Concerns about polluted environment date back to Roman times and hundreds of years to concerns over “foul” water and air in England
- Indeed, not until modern times, was air of England “cleaned up”



From Lomborg 2001; The Skeptical Environmentalist



Roots of Environmental Tox.

- Paul Muller discovers insecticidal properties of DDT
 - Wins Nobel prize in 1949
 - Used extensively during WWII
 - Domestic use grew rapidly by 1950
 - Registration suspended in US in 1973
 - Probably more research on this xenobiotic than any other



Roots of Environmental Tox.

- Rachel Carson's *Silent Spring* (1962) commonly (mythologically) considered as progenitor of environmental awareness with regard to toxics
 - Challenge: pick up a copy of *Silent Spring* and check the references
 - By the late 1940's and into the 1950's, numerous papers were published on what would now be considered environmental toxicology of DDT



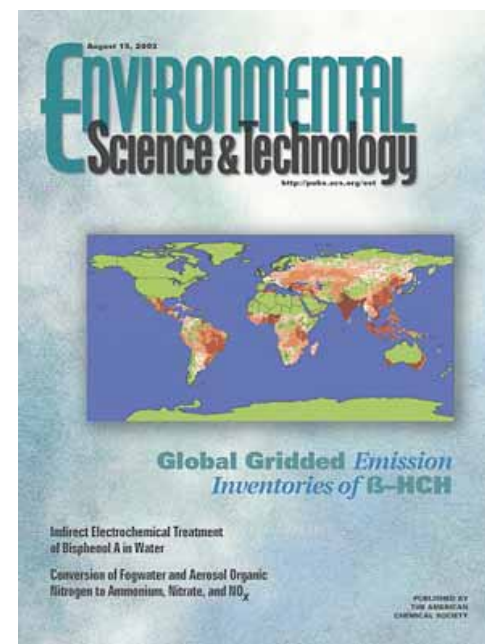
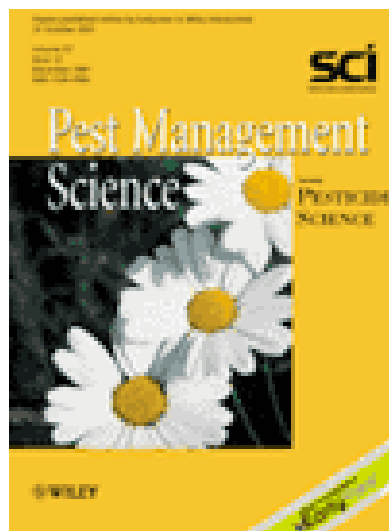
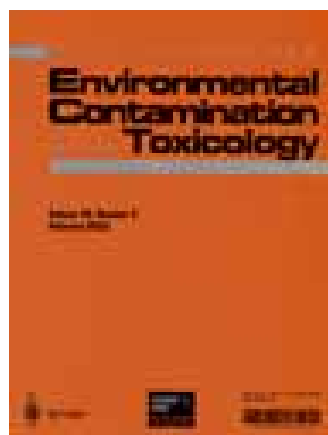
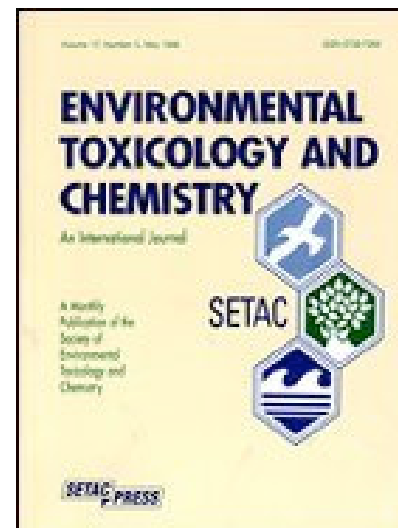
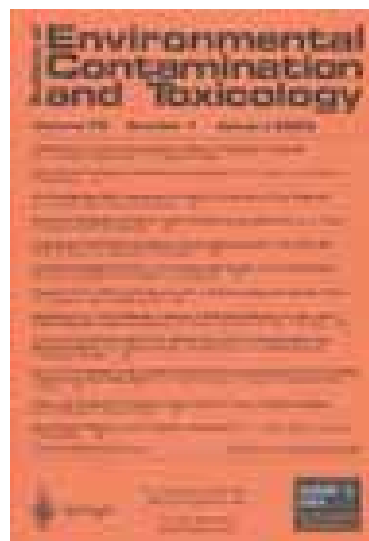
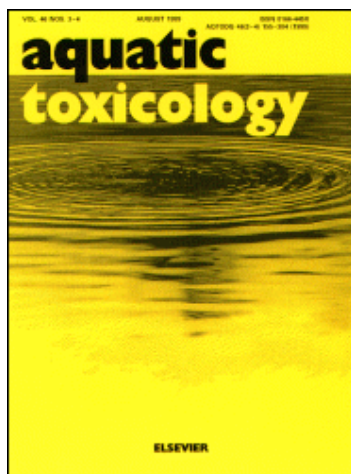
Roots of Environmental Tox.

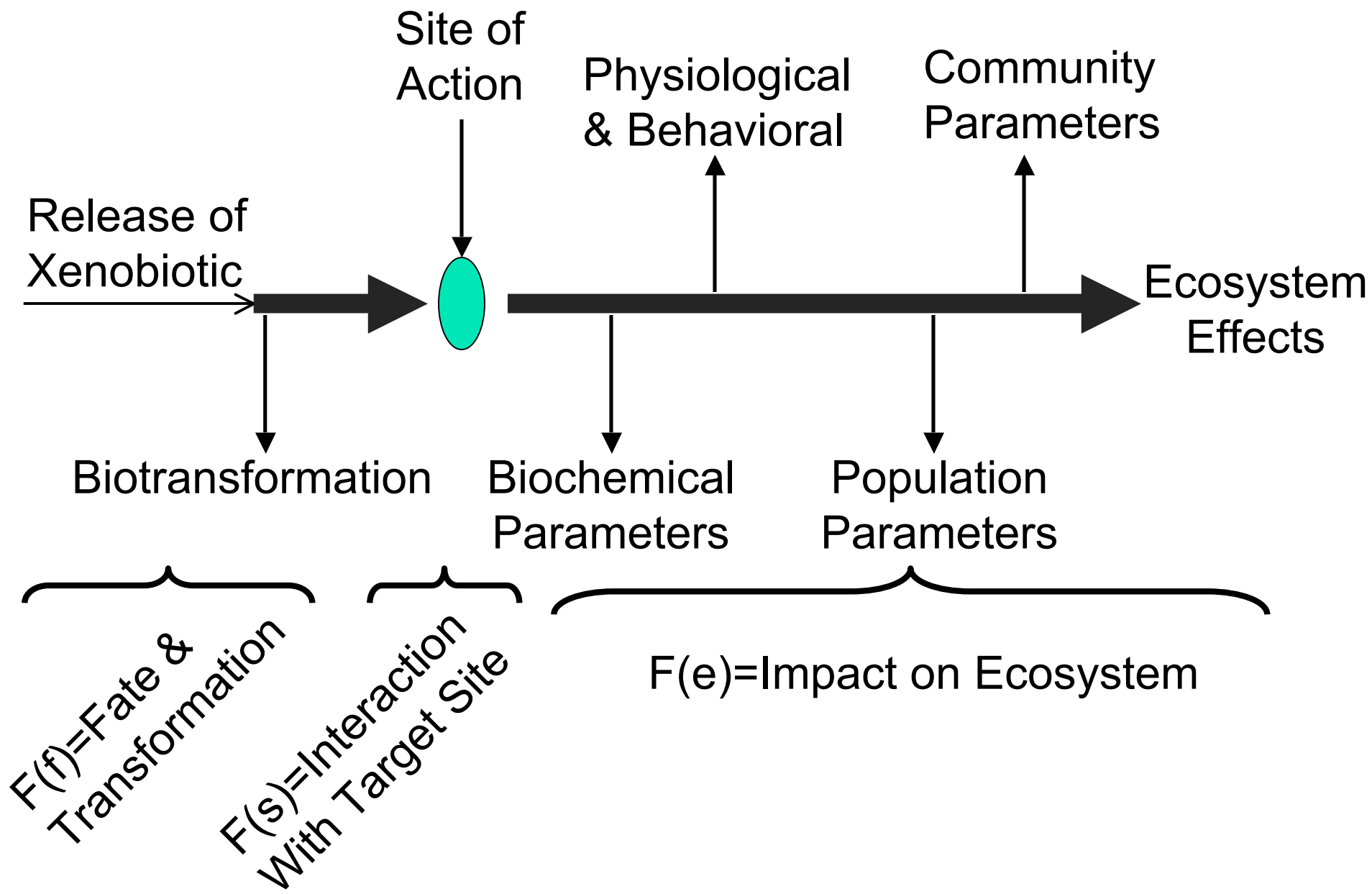
- The origination of environmental toxicology may have actually started even before the era of DDT
 - Insect toxicologists needed to know how compounds worked in the environment to control insects
 - Examination of the Journal of Economic Entomology shows major environmental toxicology themes prior to Carson's book
 - Measurement of toxicity; symptomatology, mode of action, metabolism; insecticide resistance; pesticide selectivity & comparative toxicology; insecticide residues & analytical methods; hazard evaluation; environmental chemodynamics



Sensitivity of Entomologists

- Sheppard, 1939
- Wrote book on “The Chemistry & Toxicology of Insecticides”
 - “Chemical control as the advantage that it brings prompts relief from the depredations of insects. On the other hand it is frequently only a palliative and should be accompanied by steps taken to eliminate the sources of infestation. The relation of permanent measures to the economy of other forms of natural life, however, needs full consideration. This was shown recently in the conflicting methods required for mosquito control and for wild game conservation.”





Based on Landis & Yu (1999)



Linear vs. Non-linear Thinking

- The hierarchy of events depicted by the three functions seems linear
 - i.e., it implies that there is some stable equilibrium state of the ecosystem that will return when the toxicant stressor is removed
 - If this were true, then remediation of any system would seek return of this state
- In reality, however, the ecosystem is chaotic (which means the system exhibits nonlinear dynamics), and once perturbed (naturally or synthetically) is will not return to some idealistic equilibrium state



Non-Linear Dynamics & the Community Conditioning Hypothesis

- Landis et al. have argued that the ecosystem itself, which is nonorganismal, retains a historical “memory” that interacts (gives feedback) to the organisms themselves
 - They have shown in artificial laboratory housed ecosystems (microcosms) that effects persist long after a toxicant has dissipated below known levels, suggesting that the ecosystem retains information about events that have happened within itself
 - For example, if resistant individuals gained prominence, this change in gene frequency (a biotic character) would be retained as part of the ecosystem over a long period and cause changes in the relationships between organisms
 - Must account for this complicated feedback system when making decisions about remediation



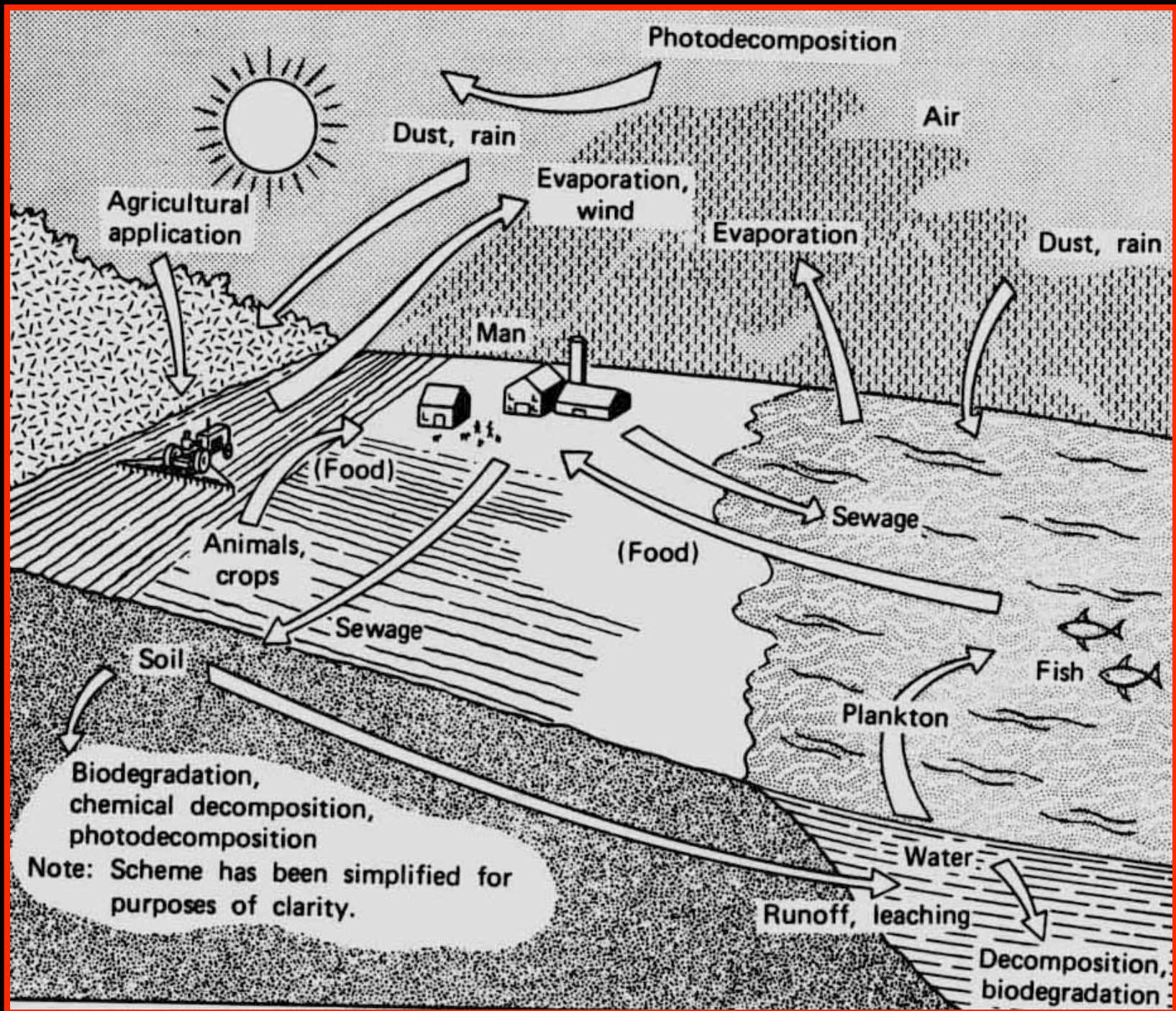
Are We Stuck with What We Can Measure

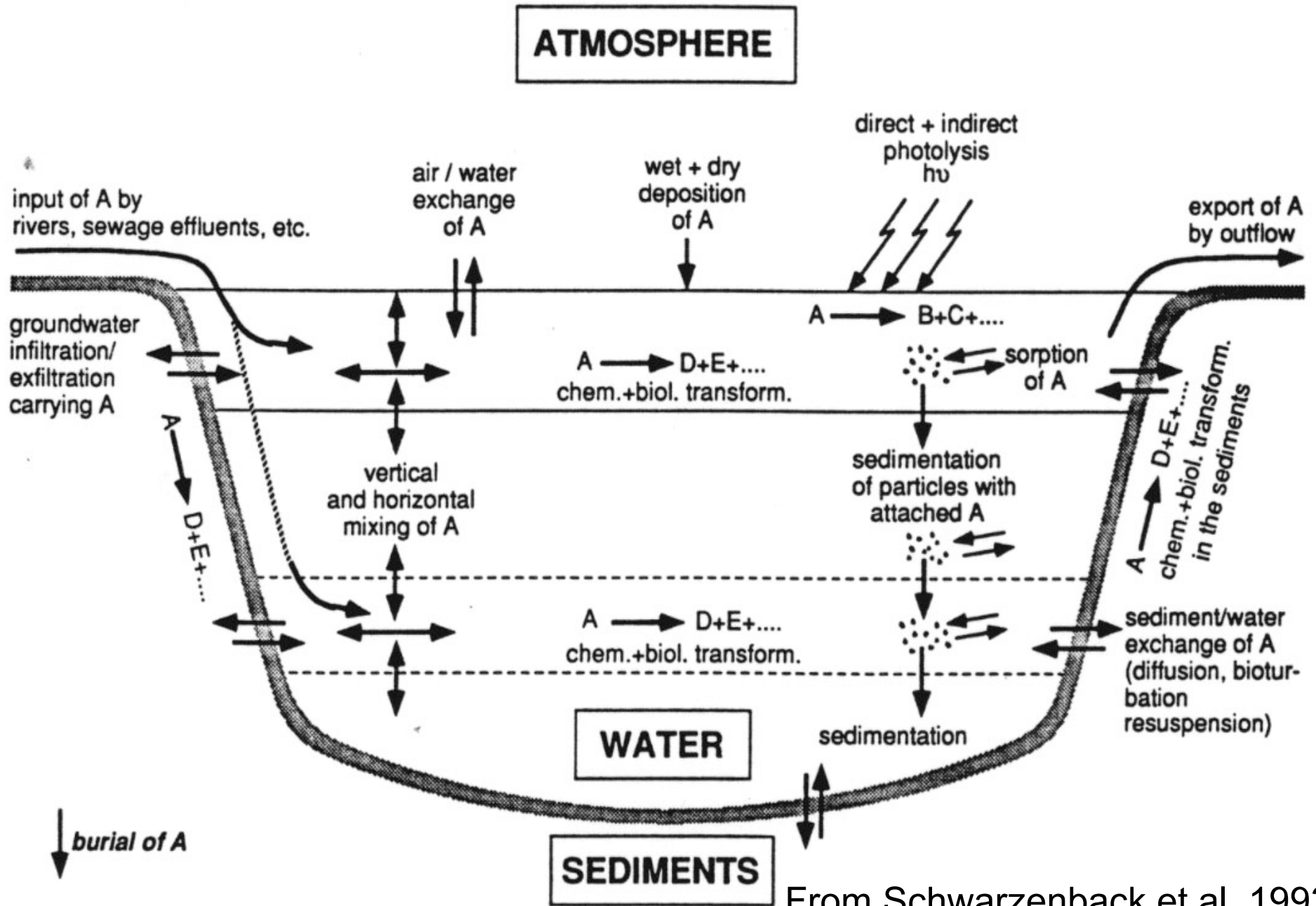
- Despite the attractiveness of the community conditioning hypothesis, we still have to deal with the three functions that can possibly lead to effects at higher levels of organization
- At least we can strive to make predictions about individuals and perhaps populations



Fortunately, We Have a Theoretical Framework

- With a theoretical framework to aid understanding the “functions” controlling toxicant-organism interactions, we can still make predictions about the likelihood of adverse effects
 - Environmental Chemodynamics
 - Pharmacodynamics/Pharmacokinetics
 - Also called toxicodynamics/toxicokinetics





From Schwarzenback et al. 1993



Environmental Chemodynamics

- Goal: prediction of adverse effects
- Objective: understand distribution of chemicals in environment that lead to potential exposure
- Holistic and based in physical chemistry
 - All is controlled by thermodynamics and kinetics
- All environmental compartments interface with one another



Environmental Chemodynamics

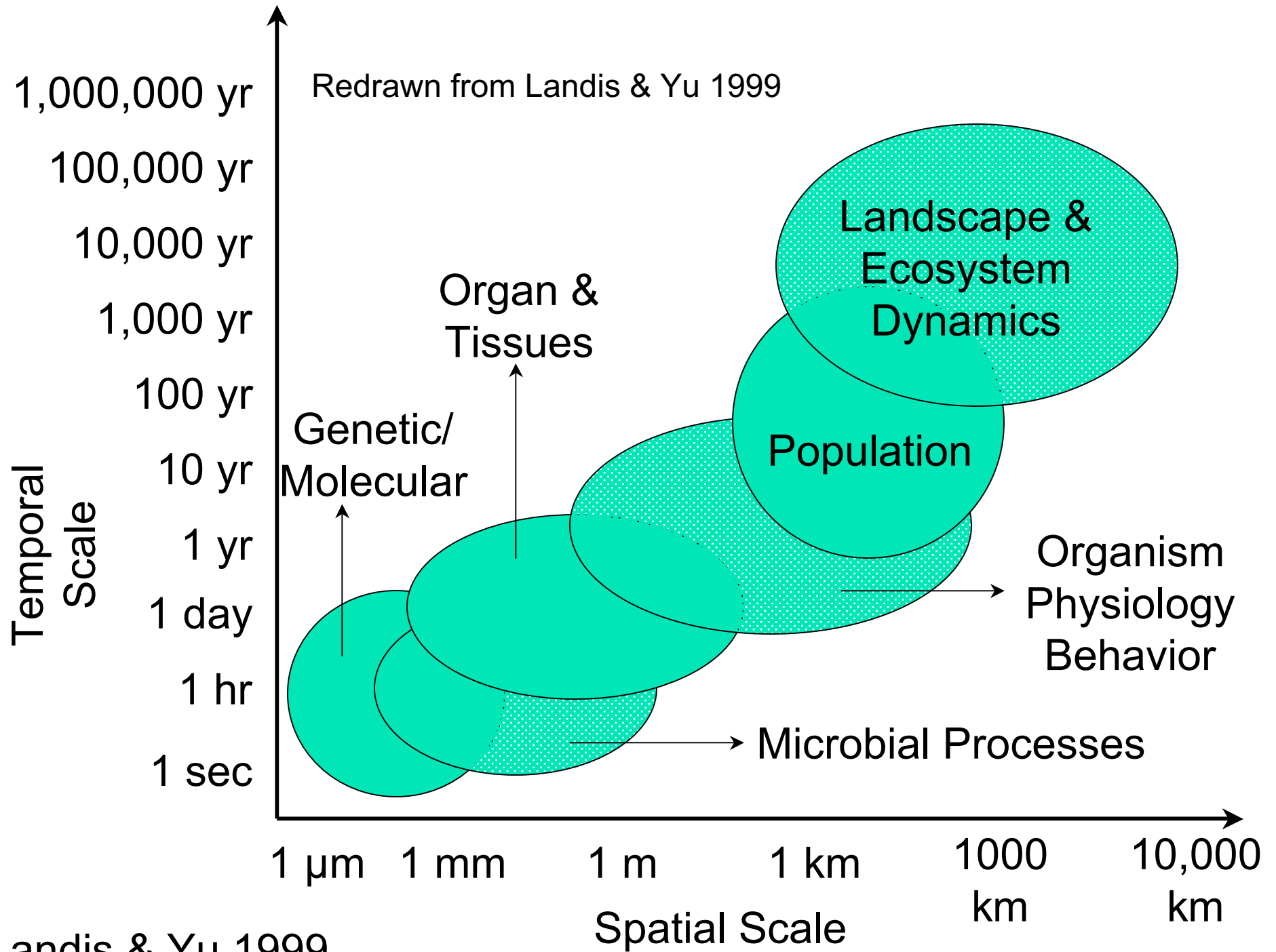
Focus Areas

- Physicochemical properties
- Partitioning
- Attenuation
- Transport
- Modelling

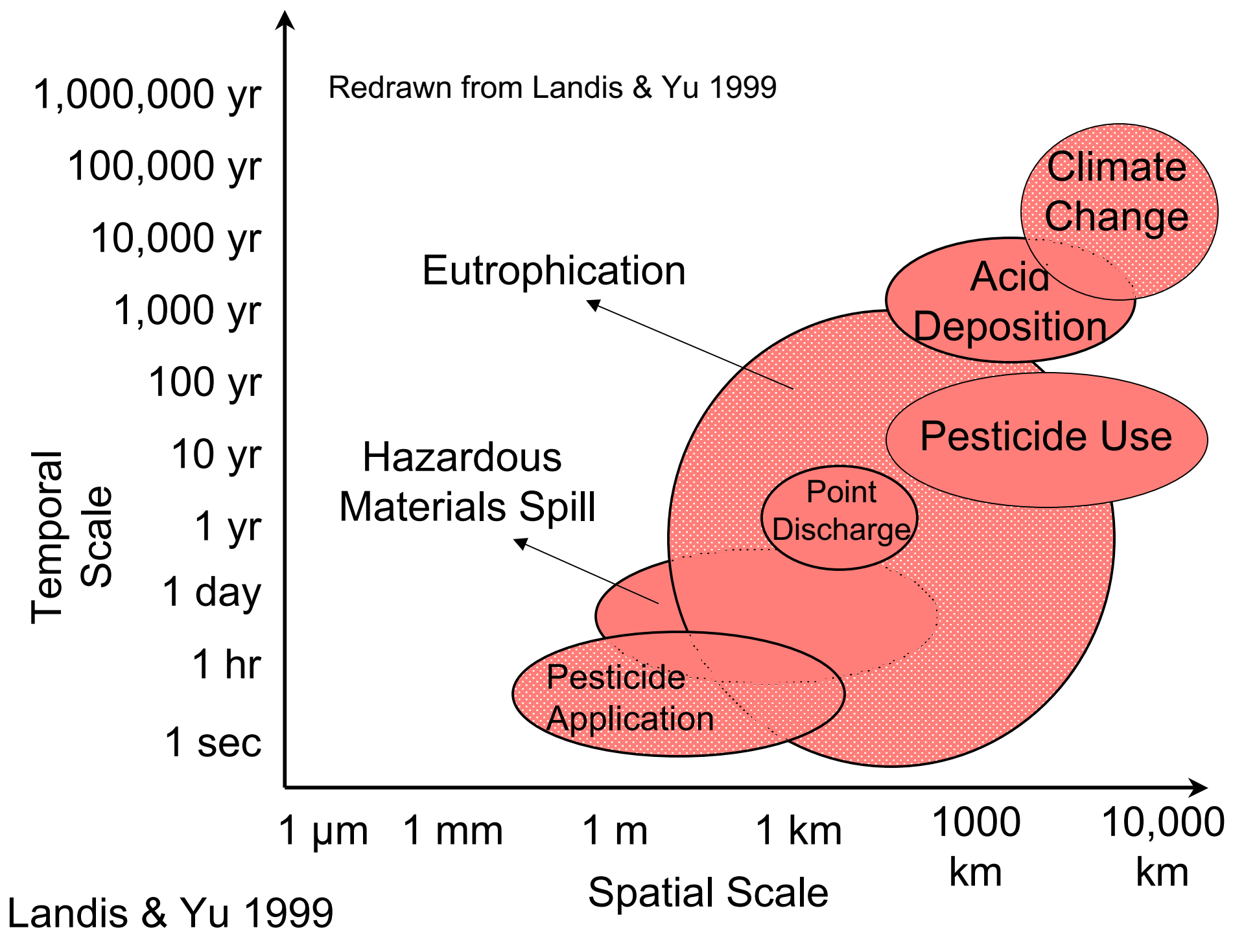


Toxicodynamics/Toxicokinetics

- Absorption rate/amount
- Distribution in the body
- Metabolism
- Excretion
- Target site interactions



Landis & Yu 1999



Lomborg 2001; The Skeptical Environmentalist

