Centrum pro výzkum toxických látek v prostředí

Ecotoxic effects
- Introduction –

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Tento projekt je spolufinancován Evropským sociálním fondem a státním rozpočtem České republiky.

EVROPSKÁ UNIE esf

MINISTERSTVO ŠKOLSTVÍ, MLÁDEŽE A TĚLOVÝCHOVY

OP Vzdělávání pro konkurenceschopnost

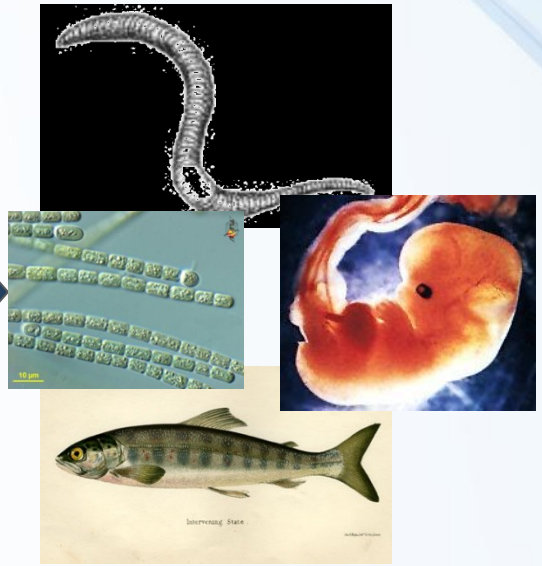
UNIVERSITAS MASARYKIANA BRUNENSIS

INVESTICE DO ROZVOJE VZDĚLÁVÁNÍ

CHEMICAL ENTERS THE ENVIRONMENT

LEVELS, FATE, PROCESSES

Bioavailable fraction



CHEMICAL ENTERS THE ORGANISM

biomonitoring

Toxicokinetics

biotransformation
bioactivation
excretion / sequestration

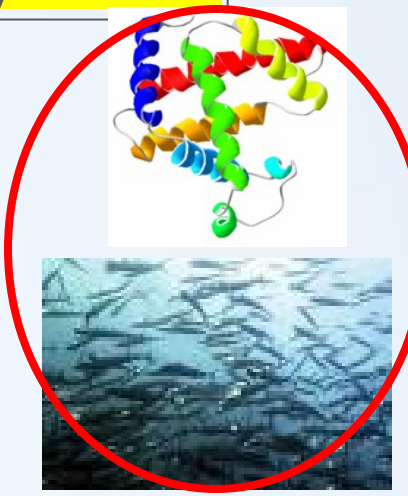
Target site

"EFFECT"
toxicodynamics

"EXPOSURE"

acute

chronic



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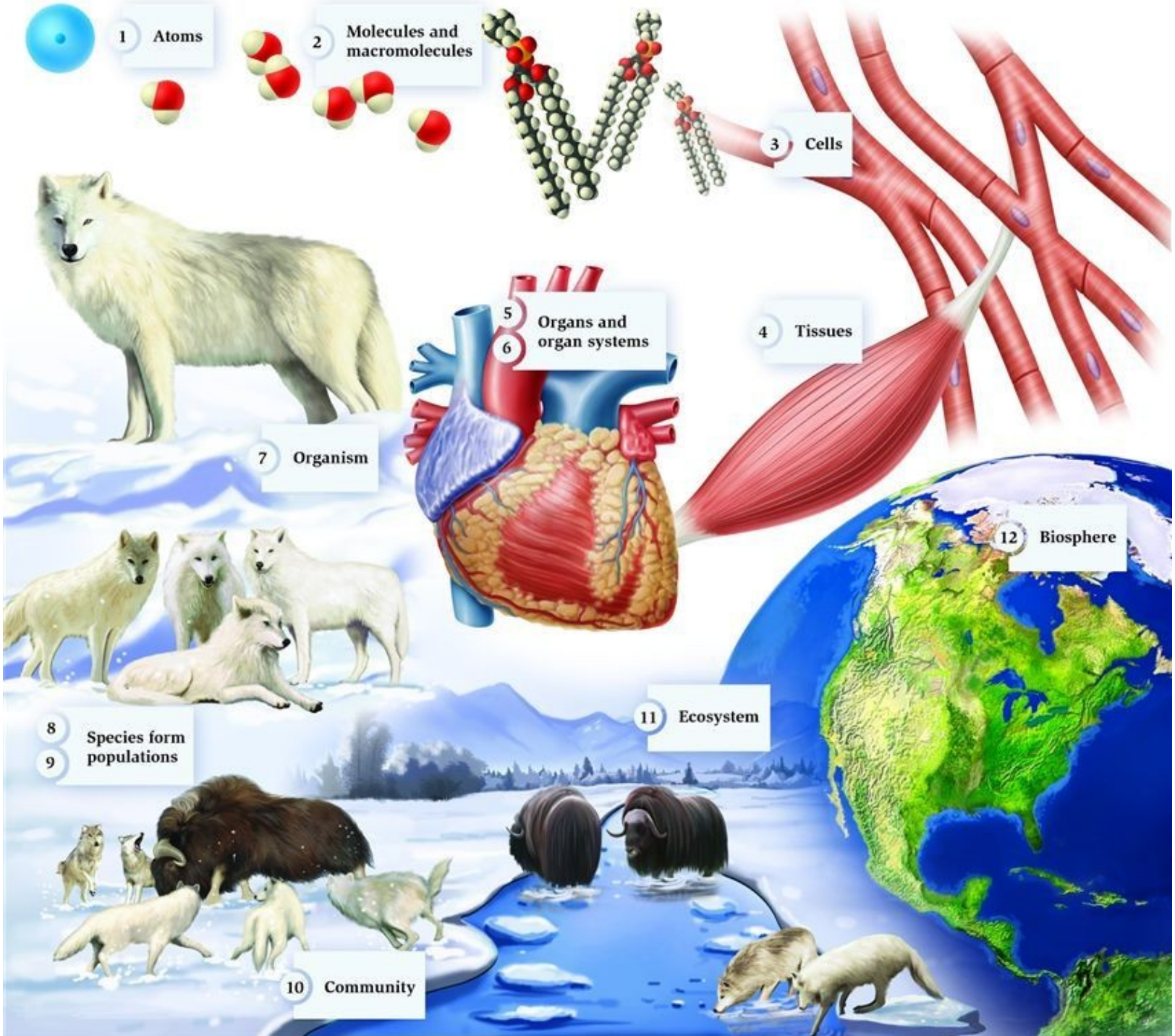
WHAT IS LIFE ?

Characteristics & properties of a living entity ?

- Structure

- Functioning



WHAT IS LIFE ?

WHAT IS ECOTOXIC EFFECT ?

Energy
hv
food

Losses
heat
faeces

Life
(*maintenance*)

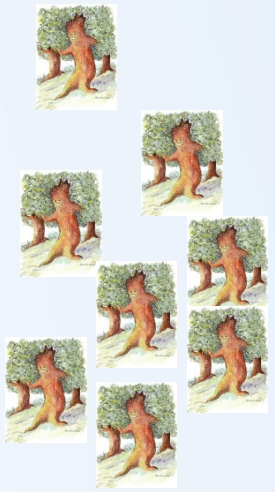
Metabolism

Control,
Interactions
with environment

Defence
against pathogens
predators …

Growth
to sexual
maturity

Reproduction



Defence against
toxicants

Chemical
stress

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v prostředí

Chemical stress
→ energy re-allocation
→ „insufficient“ resourses elsewhere

Energy
hv
food

Losses
heat
faeces

Life
(*maintenance*)

Metabolism

Control,
Interactions
with environment

Defence
against pathogens
predators …

Growth
to sexual
maturity

Reproduction

Defence against
toxicants

Chemical
stress

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v prostředí

Chemical stress

+ ... another stress (food scarcity)

Energy
hv
food

Losses
heat
faeces

Life (*maintenance*)

Metabolism

Control, Interactions with environment

Defence against pathogens predators …

Growth to sexual maturity

Reproduction

Defence against toxicants

Chemical stress

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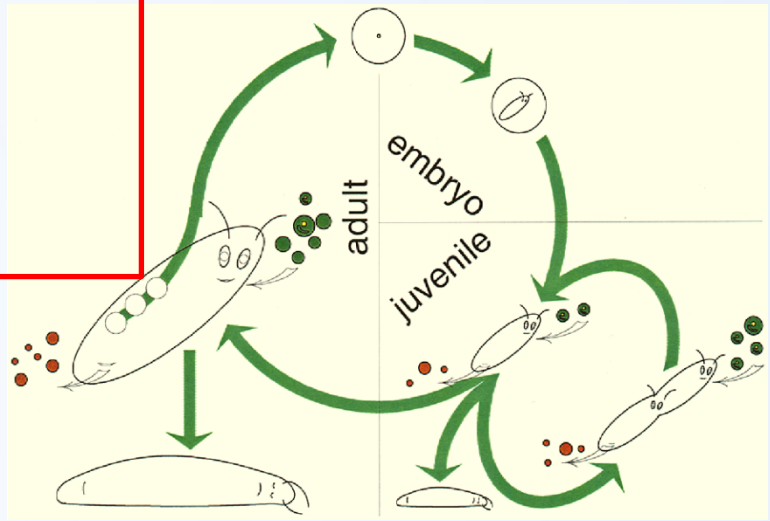
Effects at different levels - ORGANISM

Ecotoxicologicological effects (see also Bioassays)

- Effects on structure
- Effects on metabolism (maintenance)
- Effects on regulation

→Changes in functions (e.g. hormones, EE2)
→Repair, survival, **growth**
→**Death (lethality)**
→Proliferation = **Reproduction**

3 key apical endpoints
(reflected e.g. in regulations)



WHAT IS LIFE ?

WHAT IS ECOTOXIC EFFECT ?

WHAT HAPPENS „BEFORE“ EFFECT MANIFESTATION ?

WHAT ARE THE CONSEQUENCES OF THE EFFECT ?

Exposure → TK → TD → Effects

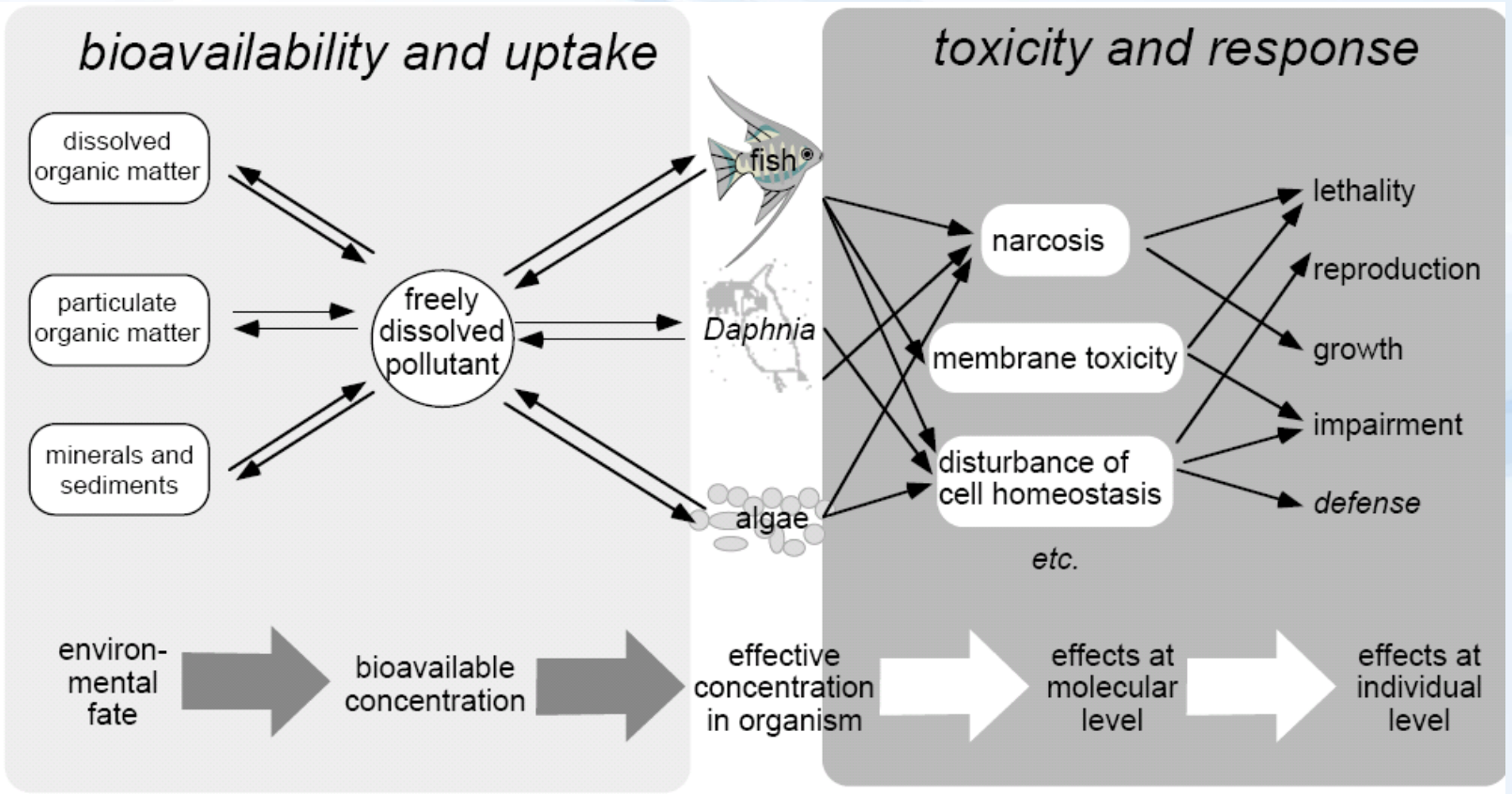


Figure 1 *The effective concentration of a pollutant in an organism (e.g. fish, daphnia, algae) or at the target site inside the organism is the link between the environmental fate of a pollutant and its toxic effect.*

Escher, B. I., Behra, R., Eggen, R. I. L., Fent, K. (1997), "Molecular mechanisms in ecotoxicology: an interplay between environmental chemistry and biology", *Chimia,* 51, 915-921.

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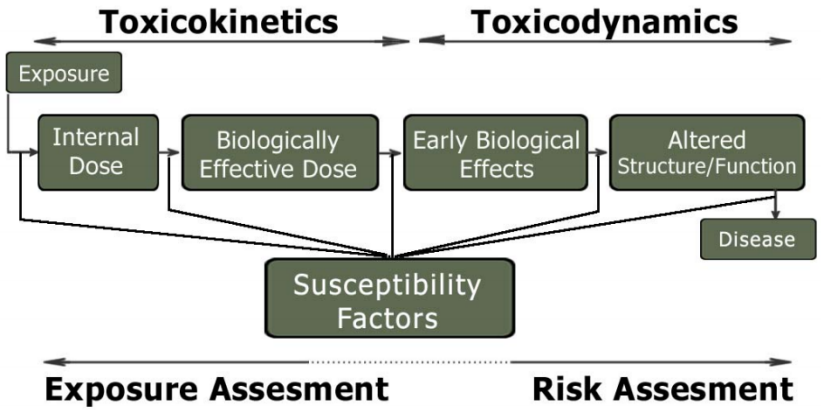
Toxicokinetics → ToxicoDYNAMICS



TARGETS = macromolecules (DNA/RNA, proteins, membrane lipids)

MoA

... and measurable EFFECTS

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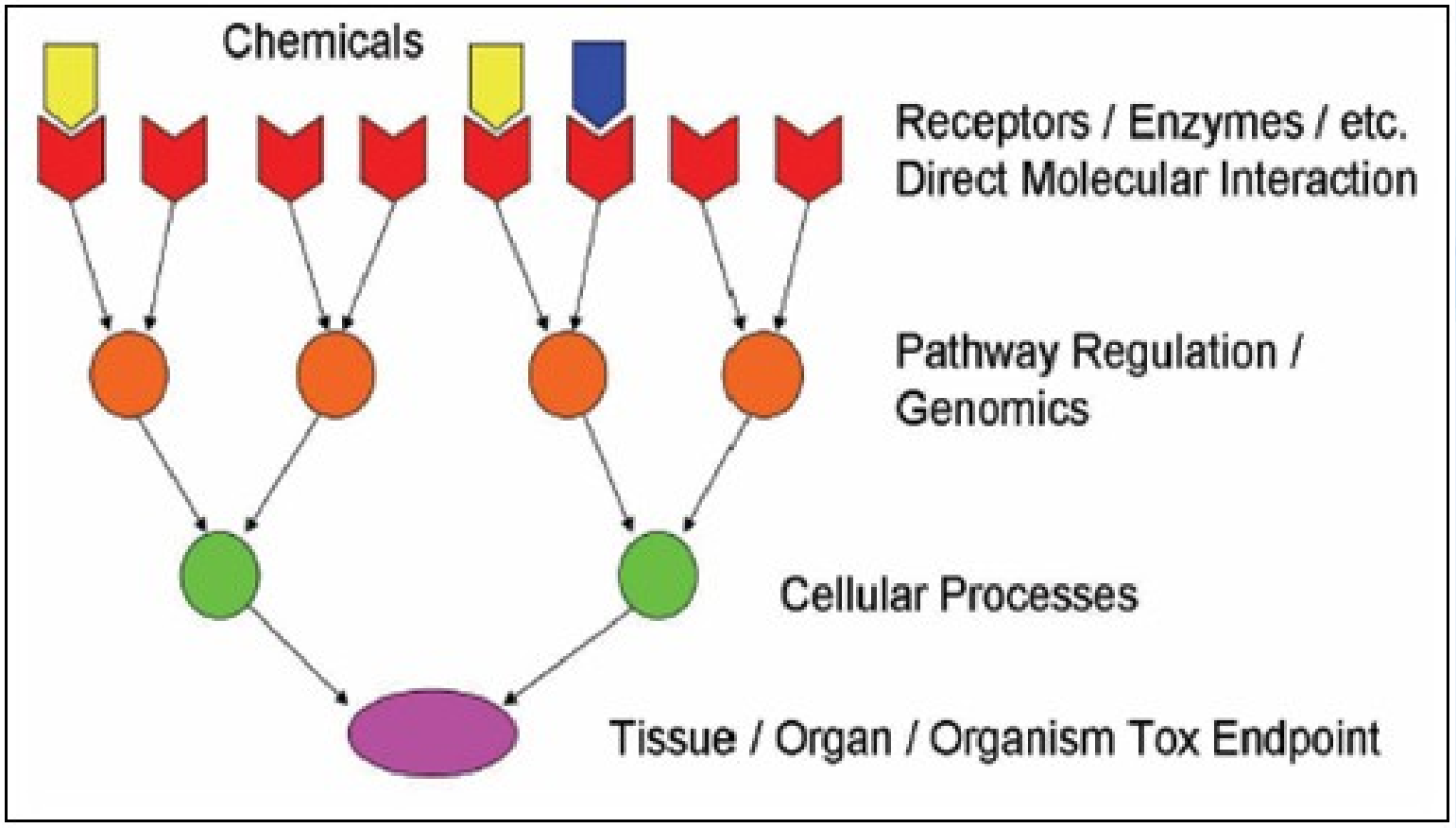
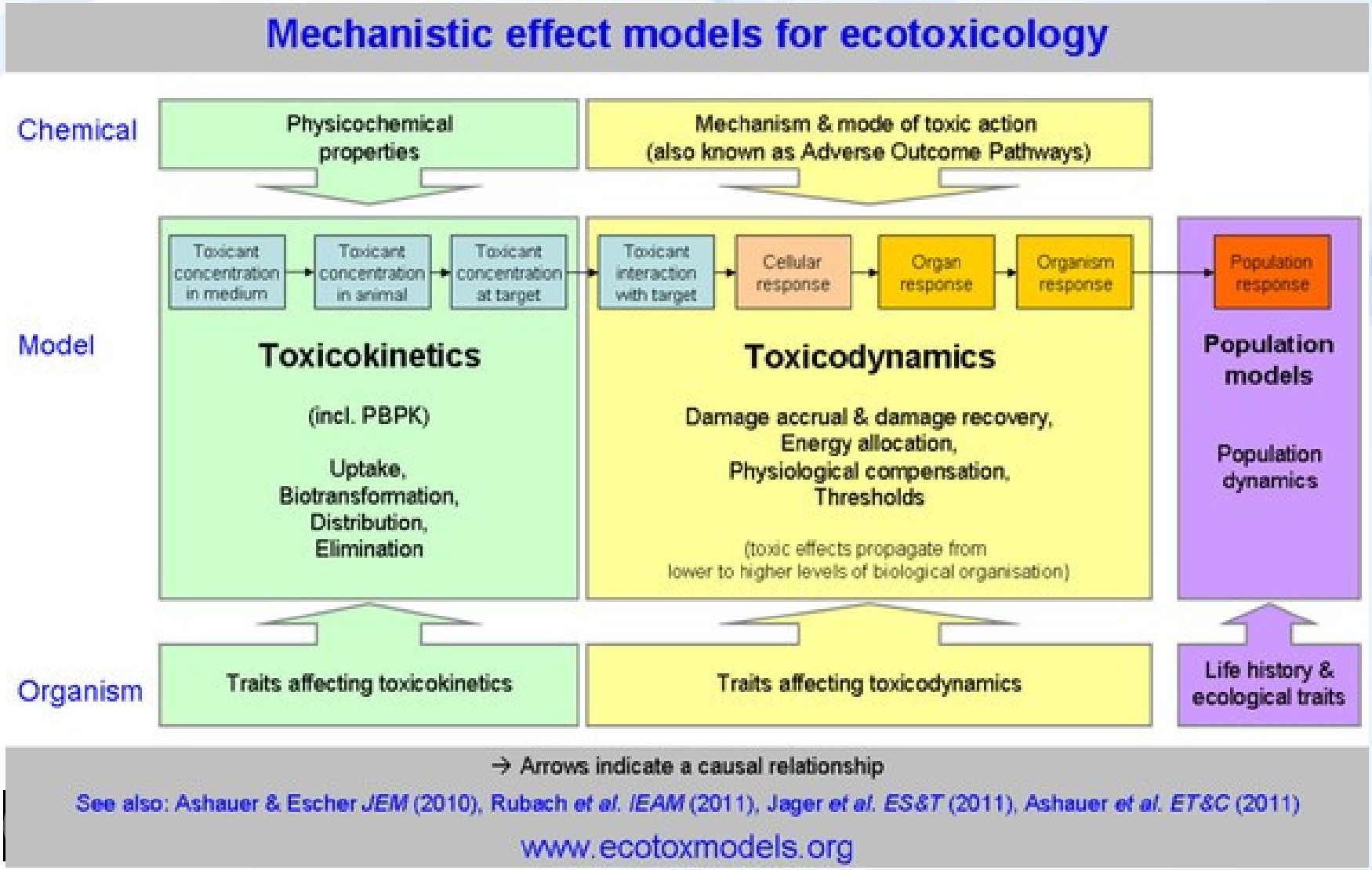
Target sites = molecules

MECHANISMS OF TOXICITY



From molecules to individuals → to populations

ADVERSE OUTCOME PATHWAYS



It all starts with MoA = Mechanisms of Action (MoA)

- According to **target molecules** (next slide)
  - Mechanisms primarily targeting different
    - BIOLOGICAL MACROMOLECULES
      - i.e. PROTEINS and/or NUCLEIC ACIDS and/or PHOSPHOLIPIDS
    - SMALL BIOLOGICAL (ORGANIC) MOLECULES
      - E.g. Antioxidants or scavengers (vit.E, GSH)

- According to **INTERACTION** between toxicant/target (next slide)
  - Non-covalent interactions
    - Partitioning (v d Waals, H-bonds, hydrophobic interactions) → [1] below
    - Partitioning with **specific steric fit** → [3] below
  - Formation of covalent bonds
    - ... with proteins / DNA-RNA / P-lipids / small molecules → [2] below

- According to **"STERIC SPECIFICITY"** of the interaction
  - NON-SPECIFIC MECHANISMS
    - the interaction between the toxicant and the target occurs "generally" with any target of certain general properties (e.g. toxicant is able to bind to ANY protein having e.g. SH- group), it does not require specific steric (structural) properties of the target
      - **mechanisms [1] and [2] below**
  - SPECIFIC MECHANISMS
    - the toxicant interacts only with certain and specific structural properties (e.g. specific binding of a pesticide into the active site of enzyme acetylcholinesterase)
      - **mechanism [3]**

Target (receptor) in MoA / toxicodynamic = BIOMOLECULE

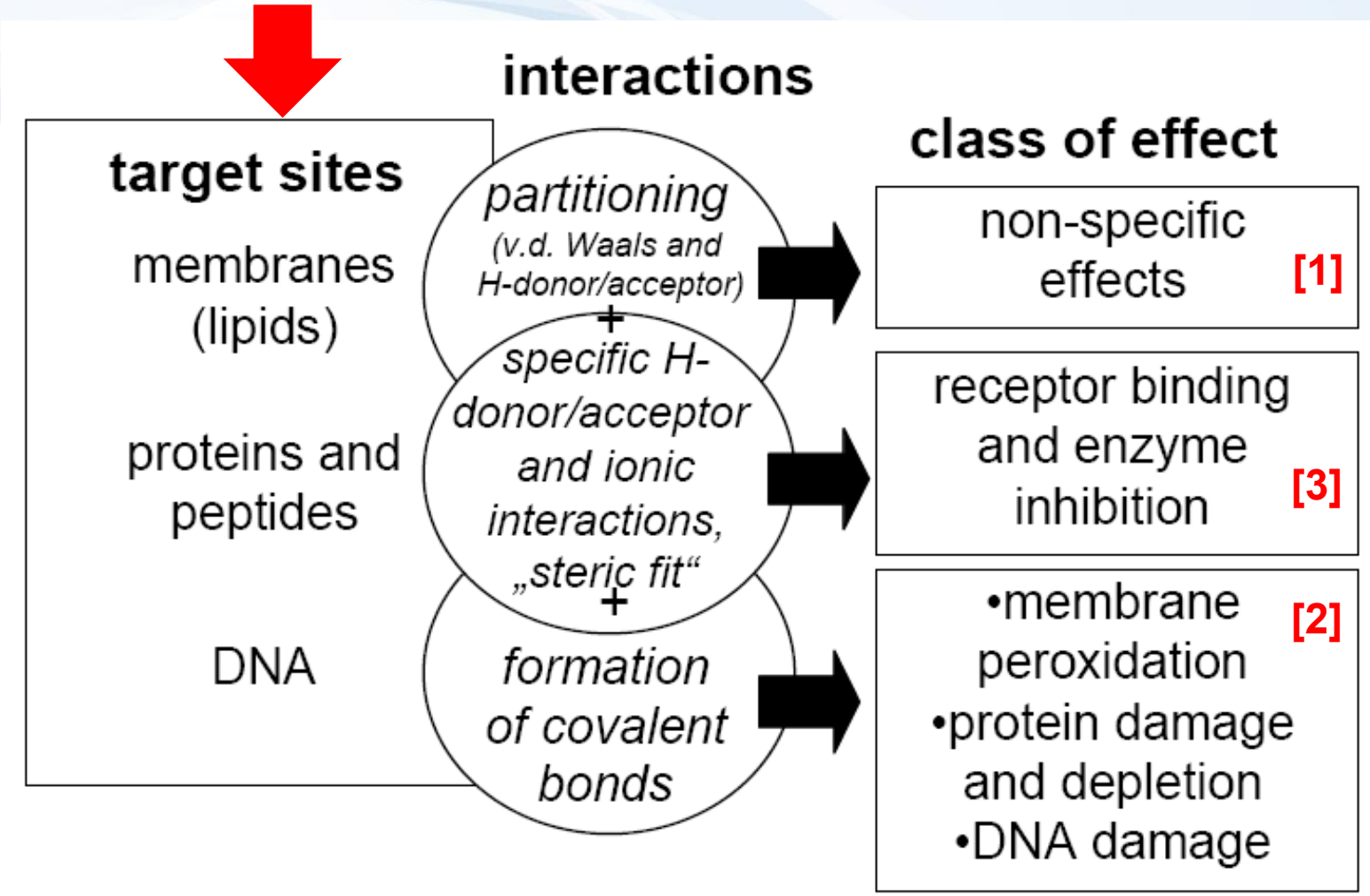


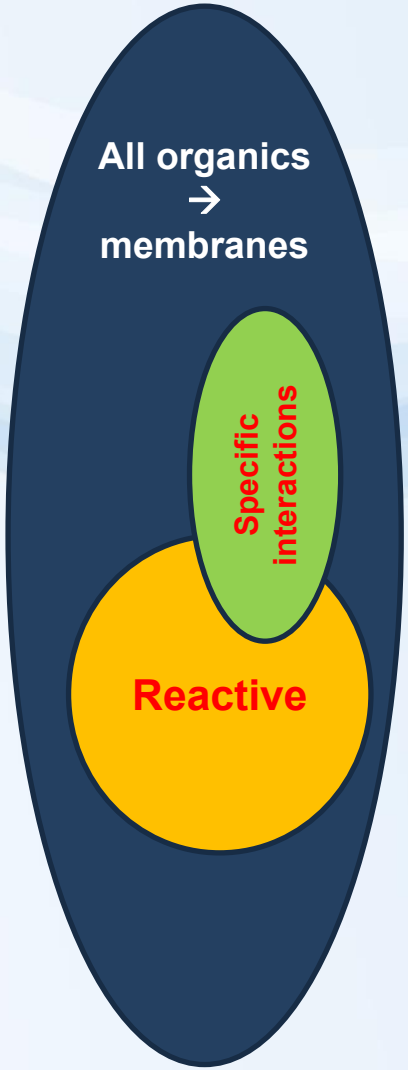
Figure 2 *Rationale behind the classification of chemicals according to mechanism: target sites and type of interaction.*

Categorizations of MoAs

- **[1] non/specific membrane toxicity**
  - Involves ALL ORGANIC compounds
  - Affinity to non-polar environment (membrane phospholipids)
  - Two types can be discriminated
    - nonpolar basal / narcotic toxicity
      - effects observed at relatively high concentrations, depends on hydrophobicity (Kow)
    - polar narcosis
      - more polar compounds may affect also membrane proteins (effects at lower concentrations than expected from Kow)

- **[2] nonspecific reactive toxicity**
  - some compounds with “reactive” properties may directly modify biological macromolecule (lipids, proteins, nucleic acids) causing thus toxic effects
  - reactive chemicals are mostly „electrophiles“ (reacting with „nucleophiles“ in cells – i.e. electrone-rich sites - nucleotides, -NH2, -SH and others), and also toxic (heavy) metals

- **[3] specific steric interactions**
  - only certain specific compounds selectively affect specific targets
  - E.g. enzyme inhibitions (drugs, insecticides); receptor interactions (e.g. Estrogens)
  - Can be non-covalent as well as covalent
  - Effects at **very low** concentrations



MoA(s) - toxicity mechanisms - overview

Student is expected to know principles and some examples of the following main types of toxicity mechanisms

- **Membrane** nonspecific toxicity (narcosis)
- **Proteins** and inhibition of enzymatic activities
- Ligand competitions – **receptor mediated toxicity**
- **DNA** toxicity (genotoxicity)
- **Complex** mechanisms
  - Oxidative stress – redox toxicity

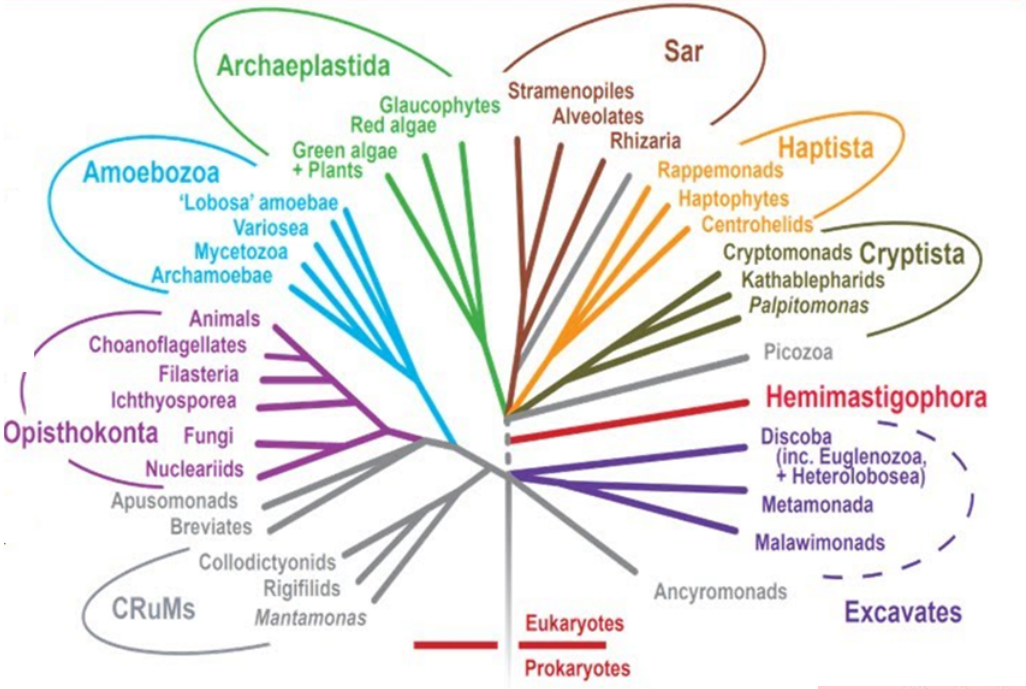
The molecular and cellular effects propagate → **ORGANISM**

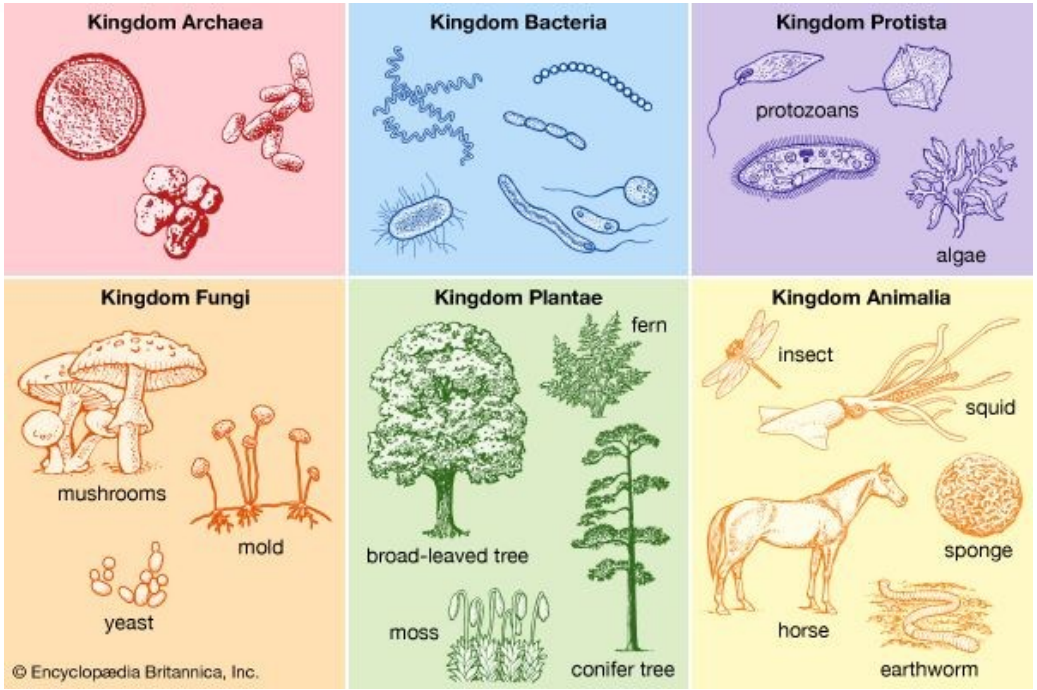
WHAT (types of) „ORGANISMS“
can be affected by ecotoxicants ?

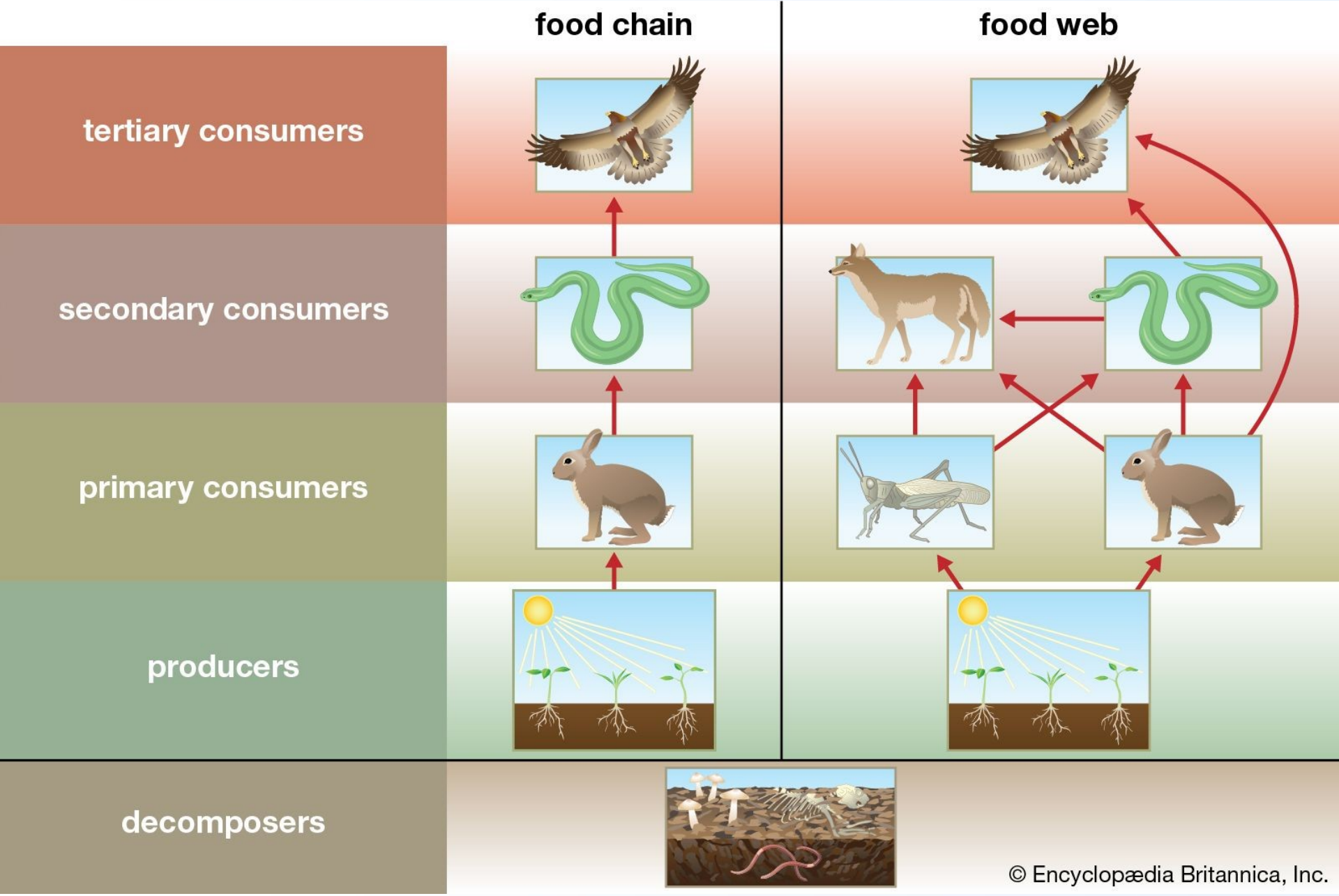
WHAT (types of) „ORGANISMS“ can be affected by ecotoxicants ?

- Structure = TAXONOMY

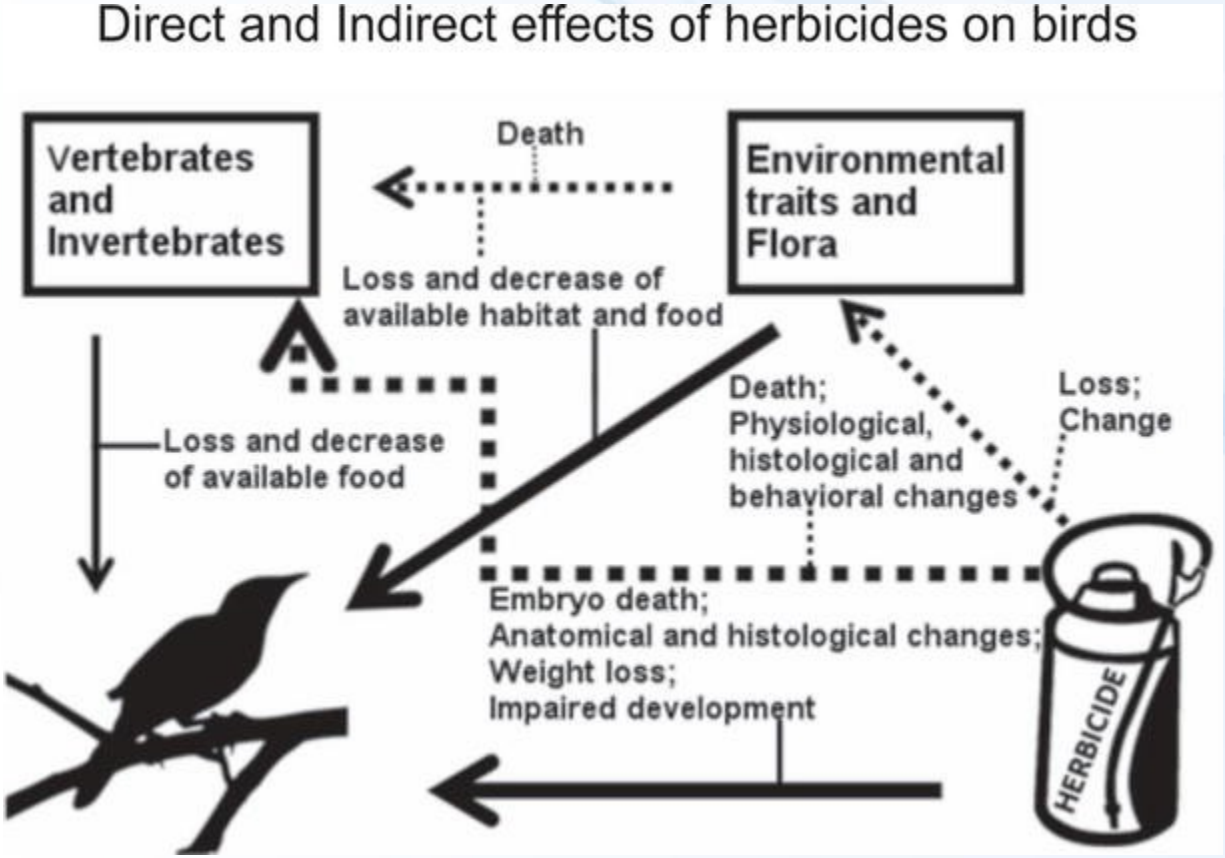
- Functioning = ECOPHYSIOLOGY


Archaeplastida
Sar
Glaucophytes
Red algae
Stramenopiles
Alveolates
Rhizaria
Green algae
+ Plants
Haptista
Amoebozoa
Rappemonads
Haptophytes
Centrohelids
'Lobosa' amoebae
Variosea
Mycetozoa
Archamoebae
Cryptomonads
Cryptista
Kathablepharids
Palpitomonas
Animals
Choanoflagellates
Filasteria
Ichthyosporea
Picozoa
Hemimastigophora
Opisthokonta
Fungi
Nucleariids
Discoba
(inc. Euglenozoa,
+ Heterolobosea)
Metamonada
Apusomonads
Breviates
Malawimonads
Collodictyonids
Rigifilids
Ancyromonads
CRuMs
Mantamonas
Excavates
Eukaryotes
Prokaryotes


Kingdom Archaea
Kingdom Bacteria
Kingdom Protista
protozoans
algae
Kingdom Fungi
mushrooms
mold
yeast
© Encyclopædia Britannica, Inc.
Kingdom Plantae
fern
broad-leaved tree
moss
conifer tree
Kingdom Animalia
insect
squid
sponge
horse
earthworm

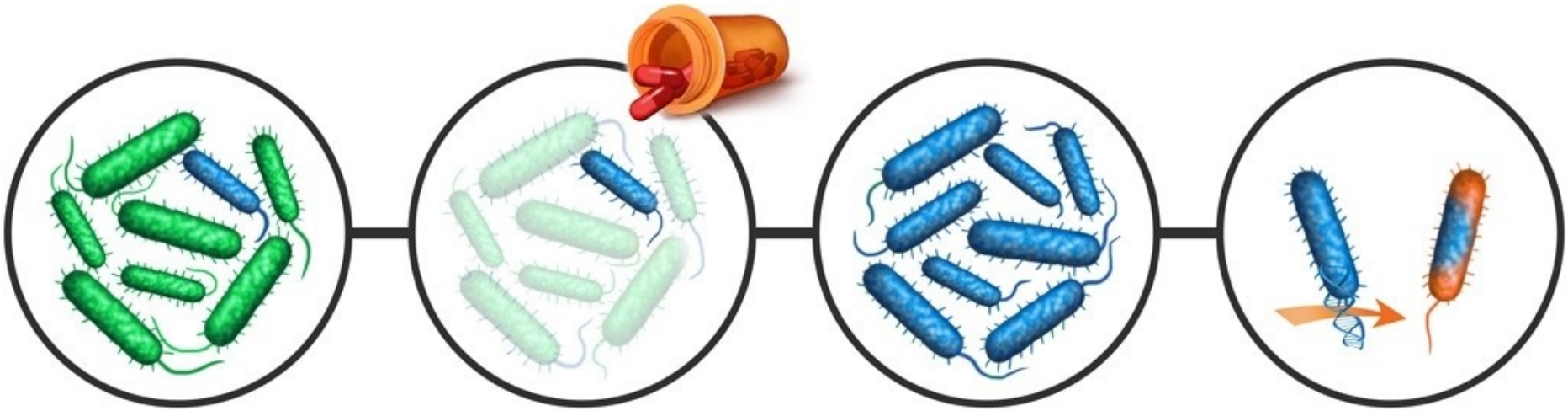


Ecotoxicity of glyphosate-based herbicide (GBH) to aquatic birds. Direct (continuous arrows) and indirect (dashed arrows) effects of GBH on birds.



https://www.intechopen.com/books/biochemical-toxicology-heavy-metals-and-nanomaterials/ecotoxicology-of-glyphosate-based-herbicides-on-aquatic-environment

Antibiotic Resistance in Bacteria



Step 1

In a population of bacteria, one bacterium mutates and becomes antibiotic resistant.

Step 2

Antibiotic kills off all bacteria except for the antibiotic resistant bacterium.

Step 3

Antibiotic resistant bacterium multiplies, forming a population of antibiotic resistant bacteria.

Step 4

Antibiotic resistant bacteria can transfer their mutation to other bacteria.

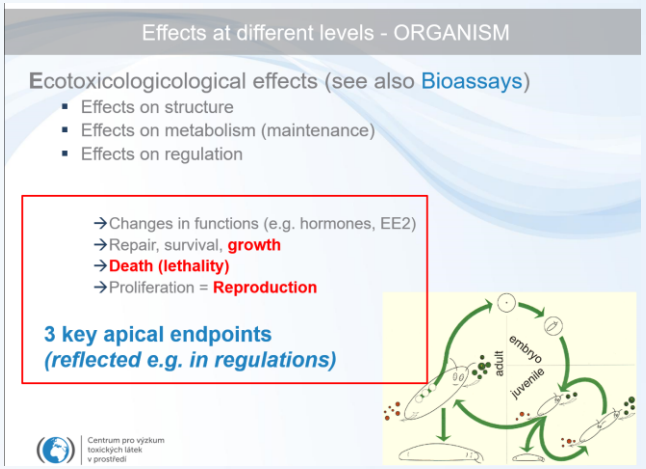
WRAP UP = TAKE HOME MESSAGE

Ecotoxicology aims to understand effects of stressors (chemicals) in biological systems

→ Be aware of **life (biological systems) in all types and dimensions**

→ (Eco)toxicological effects are captured (organized) in **Adverse Outcome Patways** – from Exposures to TK to MoA to „in vivo“ (and beyond)

→ The 3 most important biological endpoints in vivo (**apical endpoints**) reflected in pragmatic approaches (biotesting) are …



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