This is the PDF version of an animated slide presentation

SOME FIGURES MIGHT LOOK ODD AND THE VIDEOS WILL NOT WORK

PLEASE, CONTACT ME FOR THE FULL VERSION OF THE CURSE

Measuring toxicity: Concepts & Principles

https://overdoseinfo.com/caffeine-toxicity/

Measuring toxicity: Concepts & Principles

Lecturer: Abel Machado

Introduction to Pollution Science & Ecotoxicology

STUDENT ACTIVITY: A-B MONOLOGUE

Lecturer: Abel Machado

5

Measuring Toxicity: Concepts & Principles

ASSESSING TOXICOLOGICAL CAUSE & EFFECT

Skills you gain:
1- Understand the main purpose of a toxicity test
2- In-depth knowledge about assumptions when assessing potential toxicity
3- Tips to the design of your toxicity test
4- Critical evaluation the scientific and regulatory toxicity tests

Lecturer: Abel Machado

References:

youtube.com/watch?v=3-WzVJNqEuw&t=280s

How could we assess whether a novel entity is potentially harmful to ecosystems?

Toxicity testing

What are the contaminant's physical, chemical and biological structure and properties?

Where is it produced, used, transported to or disposed?

Is it degraded? How? What are the physical, chemical, and biological properties of daughter compounds?

Which physical, chemical, and biological properties of living systems could it interact with?

On which organisms and ecosystems could occur non-intended impacts?

What environmental or biological processes might emerge?

Ecotoxicological approach!

Lecturer: Abel Machado

Toxicity testing: Defining the audience

All toxicity tests aim to estimate **the potential of a contaminant** to trigger **biological responses** in an accurate and precise manner

Managers

How much can we use without casing substantial harm?

Controls represent no exposure

gadgetheat.com

OECD Common standard tests

Fundamental: scientists

It is a tool for causal inference!

What is?

Replication is pr
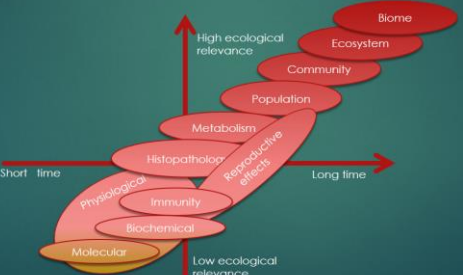
ncentration is controlled

DOI 10.15252/embj.201592958
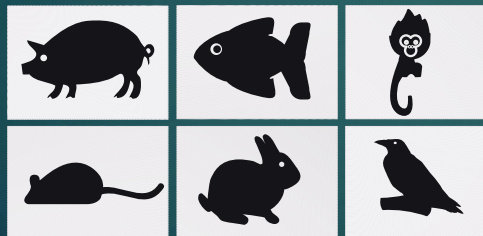
Any specific test possible

Time

Defining the toxicological context

How does our ecotoxicological model compare to other organism?
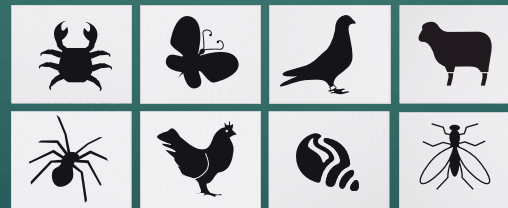
Toxicology

Human health

Multiple species models for one species

Environmental Toxicology

Any organism's health

Acute & Chronic

Multiple species models for several species

Ecotoxicology

Ecosystem health

Multiple species models for biosphere

In vitro, In vivo, Mesocosms & Field trials

Defining the context of our toxicity data

In vitro
Sub-organismal exposure

Carrot roots in culture

In vivo
Organismal exposure

Lettuce in hydroponic culture

Mesocosms
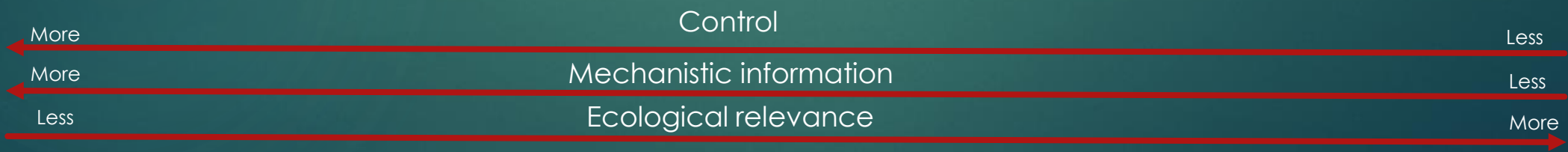Multiple organisms & species

Soil and rhizosphere microbiomes

Field trials
Exposure under realistic variability

Field work with multiple stressors planned

Control
More ← Less

Mechanistic information
More ← Less

Ecological relevance
Less → More

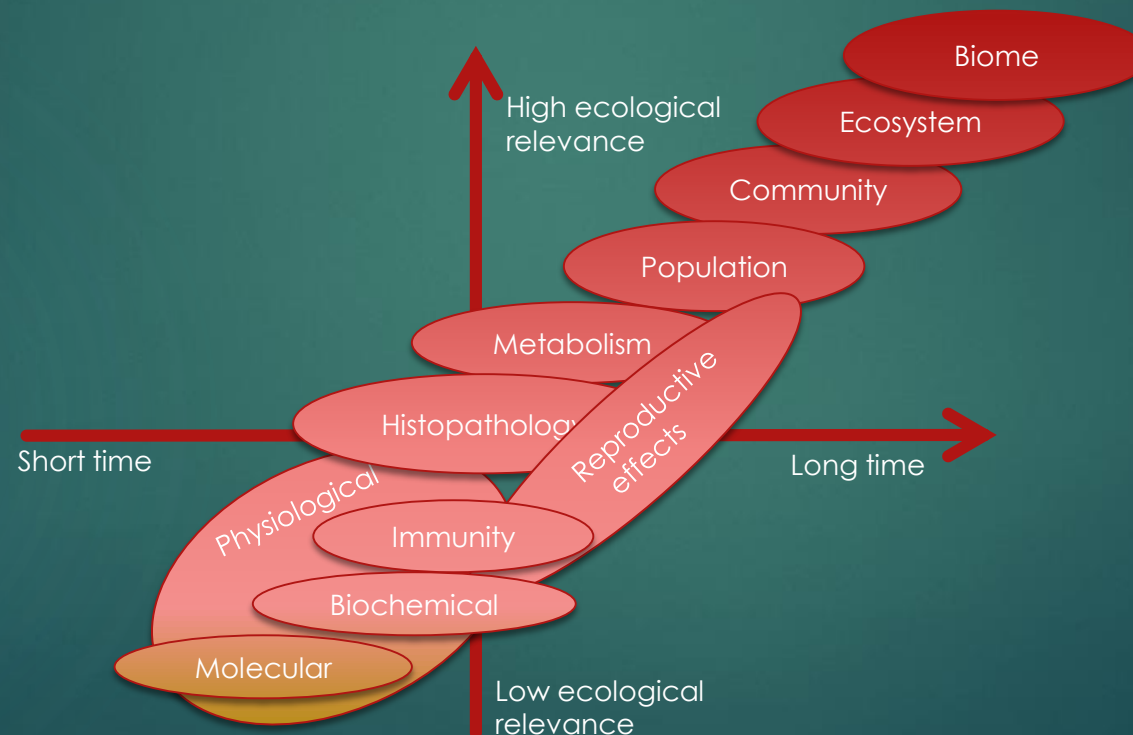# Defining the context of our data in terms of Biological Responses

Biological responses

Is it a **general biological response** or an **early quantitative sub-organismal** responses to exposure or effect associated to a particular stressor?

Student activity (Group):
Discuss what could be the context of your toxicity test in terms of:
1- Audience
2- Toxicological context
3- Environmental realism
4- Biological hierarchy
5- Data types

High ecological relevance

Biome

Ecosystem

Community

Population

Metabolism

Histopathology

Reproductive effects

Short time

Long time

Physiological

Immunity

Biochemical

Molecular

Low ecological relevance

Data types

- Quantal or binary (e.g. living= Y or N)
- Continuous (e.g. growth rate)
- Discrete
    - Nominal (e.g. male, female)
    - Ordinal (1st, 2nd, 3rd)
    - Interval

Lecturer: Abel Machado

Toxicity testing: Important metrics

A good toxicity test **MUST** control any possible influence on exposure and endpoint

Bugs bunny & Ether intoxication

Toxicant: Ether
Amount: 1 bottle
Environment: Lab
Bunny weight: ~ 2 Kg
Ventilation rate: 60 breath/ min
Tidal volume: 20 mL of air

Endpoint: A particular quantitative outcome of toxic exposure

E.g. time to sleep

Concentration: The level of (environmental) exposure to a particular toxic

E.g. 1 bottle of ether/ lab room

Exposure: The interaction between concentration, time, and other important variables affecting bioavailability
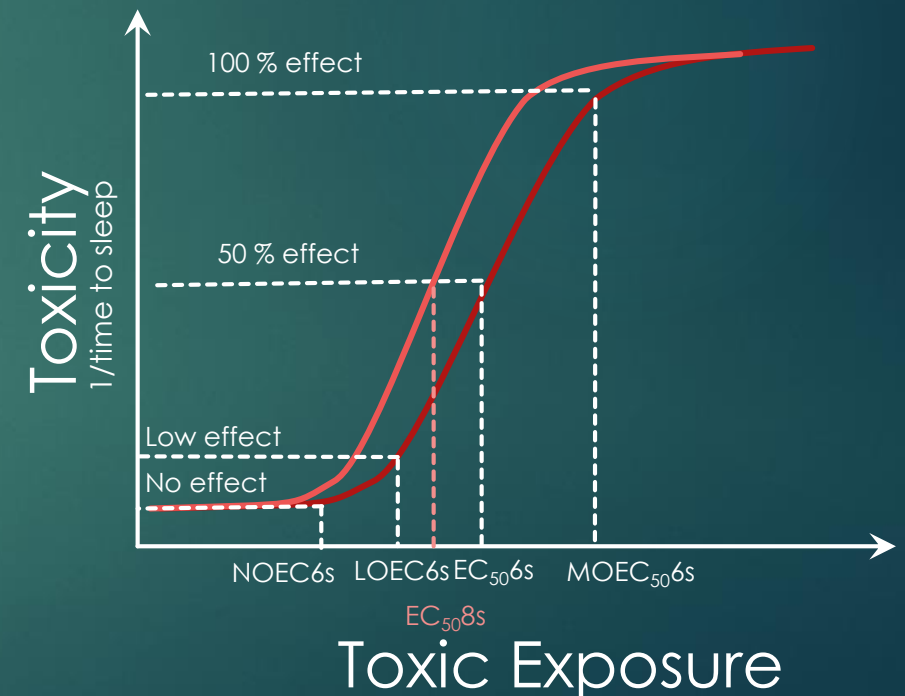
E.g. 1 bottle of ether/ lab room during 4 s (bunny), 6 s(scientist)

Dose: The effective exposure, often per mass of metabolic active tissue. 20mL air/ beath, 30-60 breath/ min, 2kg
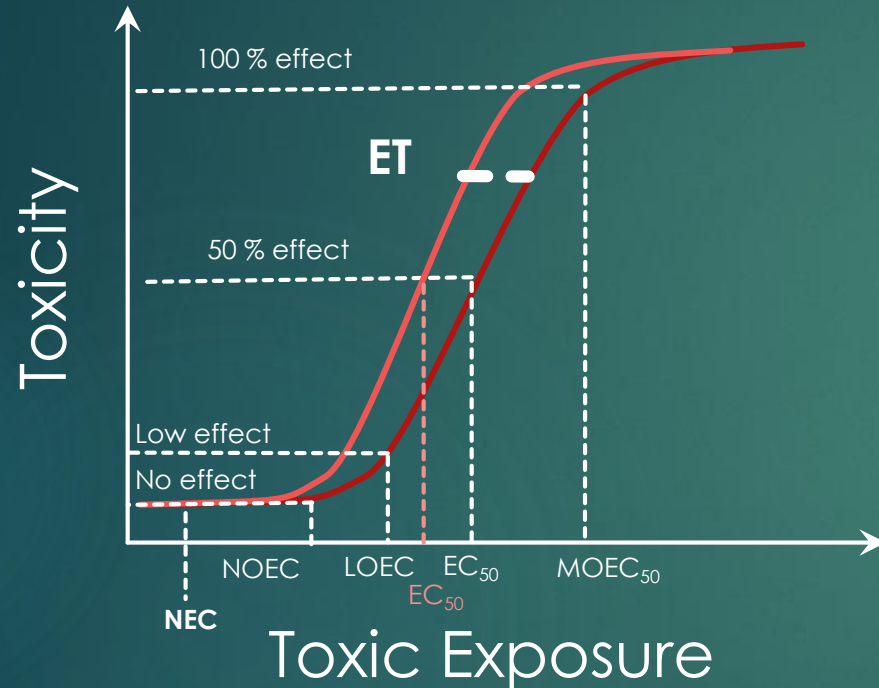
60 mL ether air/ kg (bunny) (what about the scientist?)

We need to obtain a dose-response curve if:

We want to link exposure & effects
We want to compute safe levels ±
We want to compute toxic levels ±

100 % effect

50 % effect

Low effect

No effect

Toxicity
1/time to sleep

Toxic Exposure

$NOEC6s$ $LOEC6s$ $EC_{50}6s$ $MOEC_{50}6s$

$EC_{50}8s$

Principles of dose-response estimation

Valid for the standard assumption that responses are monotone for a particular stress

100 % effect

ET
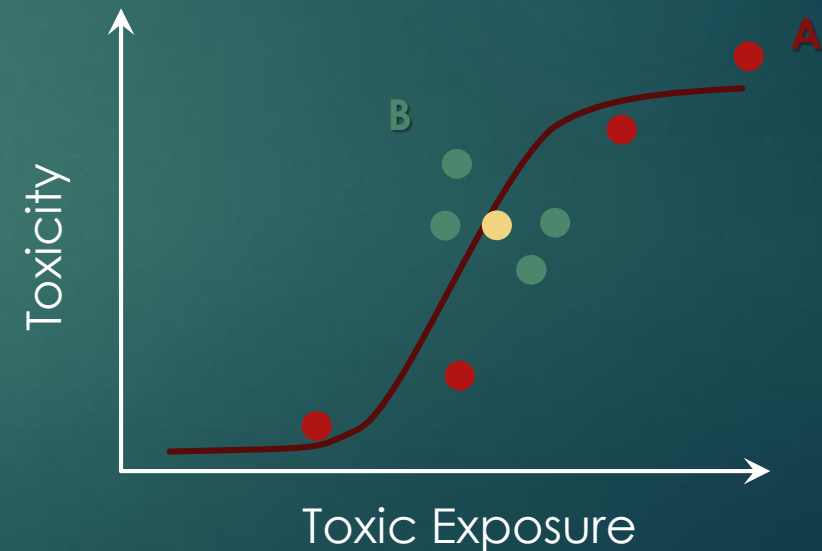
50 % effect

Low effect

No effect

Toxicity

NOEC   LOEC EC_{50} $MOEC_{50}$

EC_{50}

NEC

Toxic Exposure

NOEC = No observed effect concentration
NEC = No effect concentration

Student activity: What could be the best scenario for dose-response estimation A or B?

Ideally controls should not be exposed

● **Experimental unity (replicate):** smallest unit of an experiment to which a treatment can be allocated independently (it can contain multiple samples)
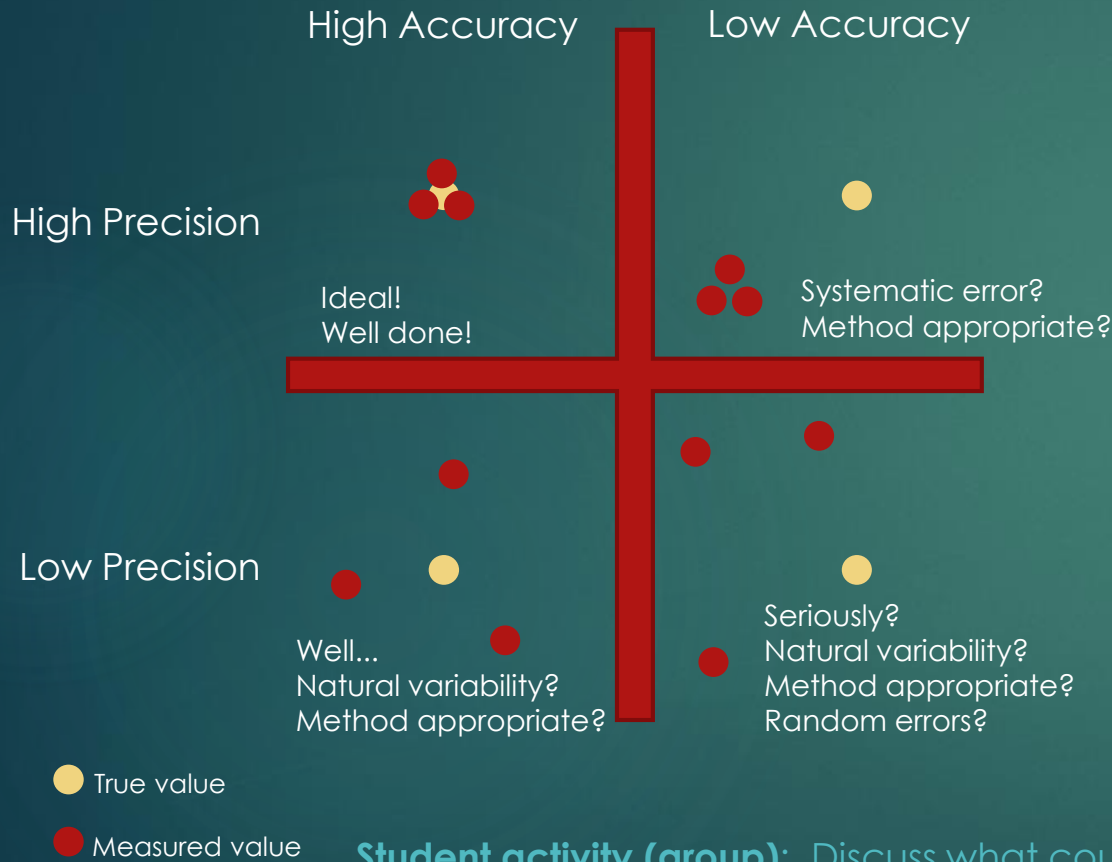
Extrapolation vs Interpolation: refers to predicting the value of variates outside or within the range of observations


A

B

Toxicity

Toxic Exposure

Principles of dose-response estimation

We want our estimated values to be **Accurate** and **Precise**

High Accuracy   Low Accuracy

High Precision

Ideal!
Well done!

Systematic error?
Method appropriate?

Low Precision

Well...
Natural variability?
Method appropriate?

Seriously?
Natural variability?
Method appropriate?
Random errors?

● True value

● Measured value
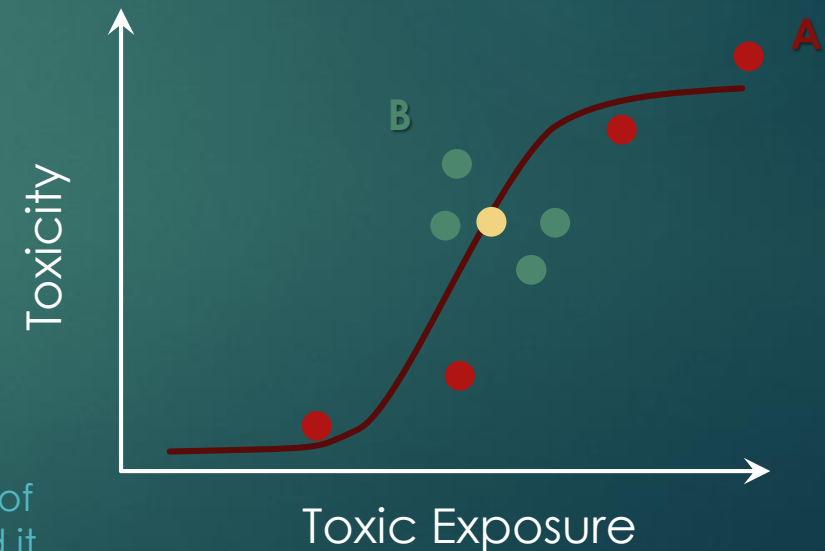
Student activity (group): Discuss what could be the causes of losses in accuracy or precision in your test and how to avoid it

Student activity: Let's make a list of the mistakes we can avoid!

Ideally controls should not be exposed

● **Experimental unity (replicate):** smallest unit of an experiment to which a treatment can be allocated independently (it can contain multiple samples)

Extrapolation vs Interpolation: refers to predicting the value of variates outside or within the range of observations

A

B

Toxicity
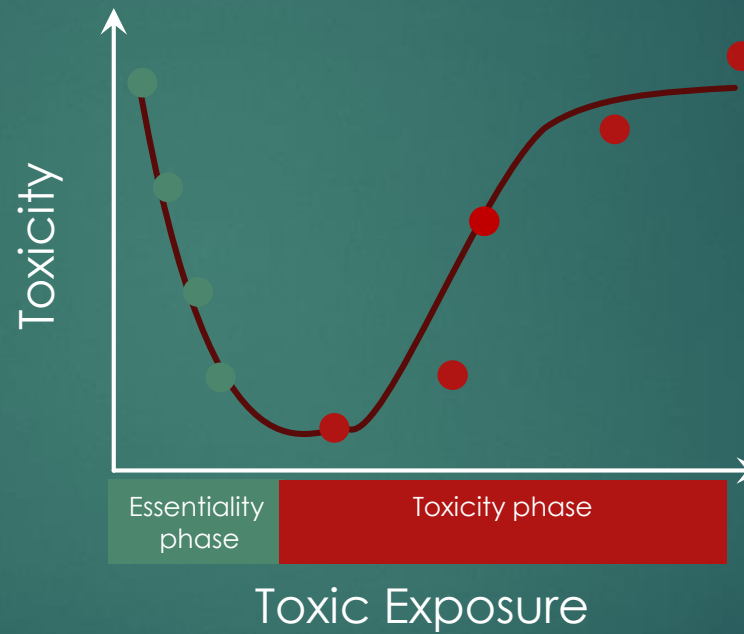
Toxic Exposure

Hormesis & Nonmonotone

When we are not accessing a monotonic response

Toxicity of a non-essential metal
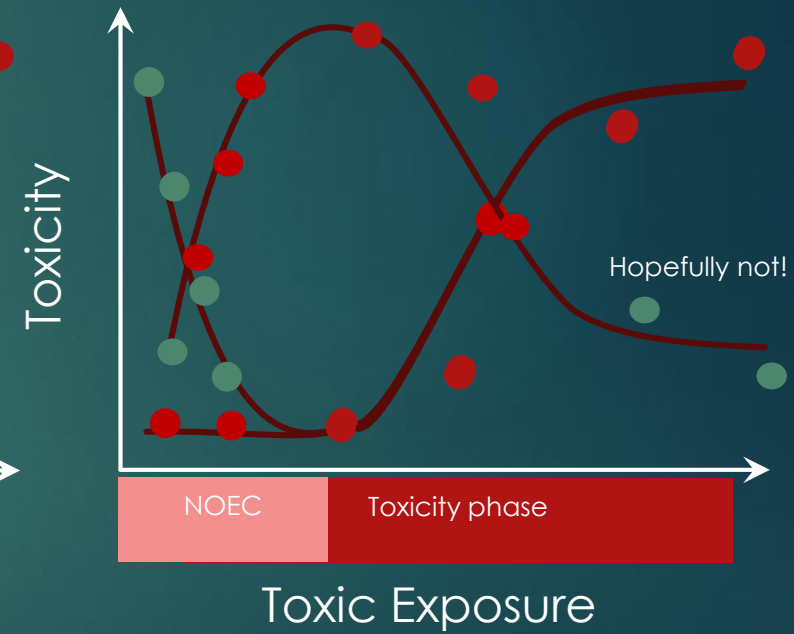Toxicity of Cd
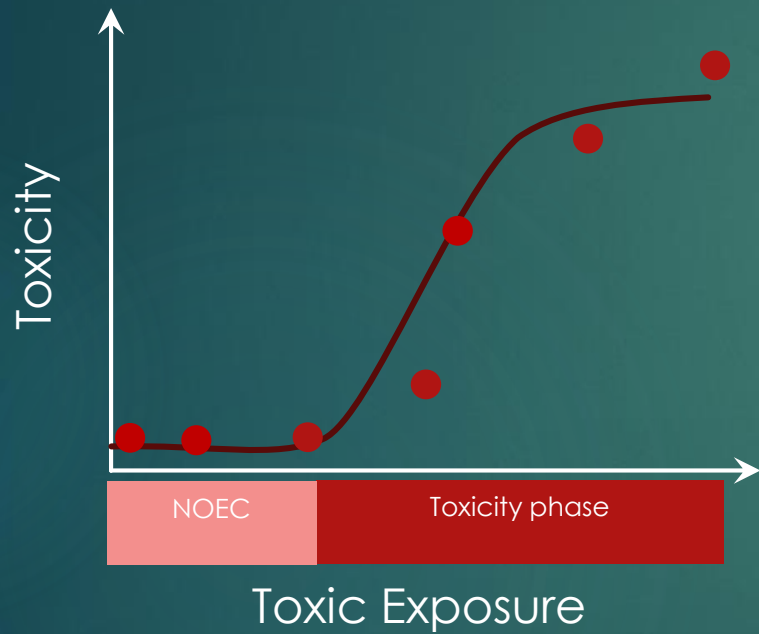
Ideally controls should not be exposed to any levels

Toxicity of an essential metal
Toxicity of Cu

Ideally controls should be exposed to essential levels

Toxicity of xenobiotics
Toxicity of Caffeine

Ideally controls should not be exposed to any levels

Student activity (group): Discuss which shape to expect for the toxicity of nanoplastics?
How would your group distribute the experimental units to assess the effect?

Toxicity of mixtures of contaminants

When things get a bit complex

Types of dose-responses to mixtures

A + B

A   A + B   B   A + B

Toxicity

NOEC   Toxicity phase

NOEC   Toxicity phase
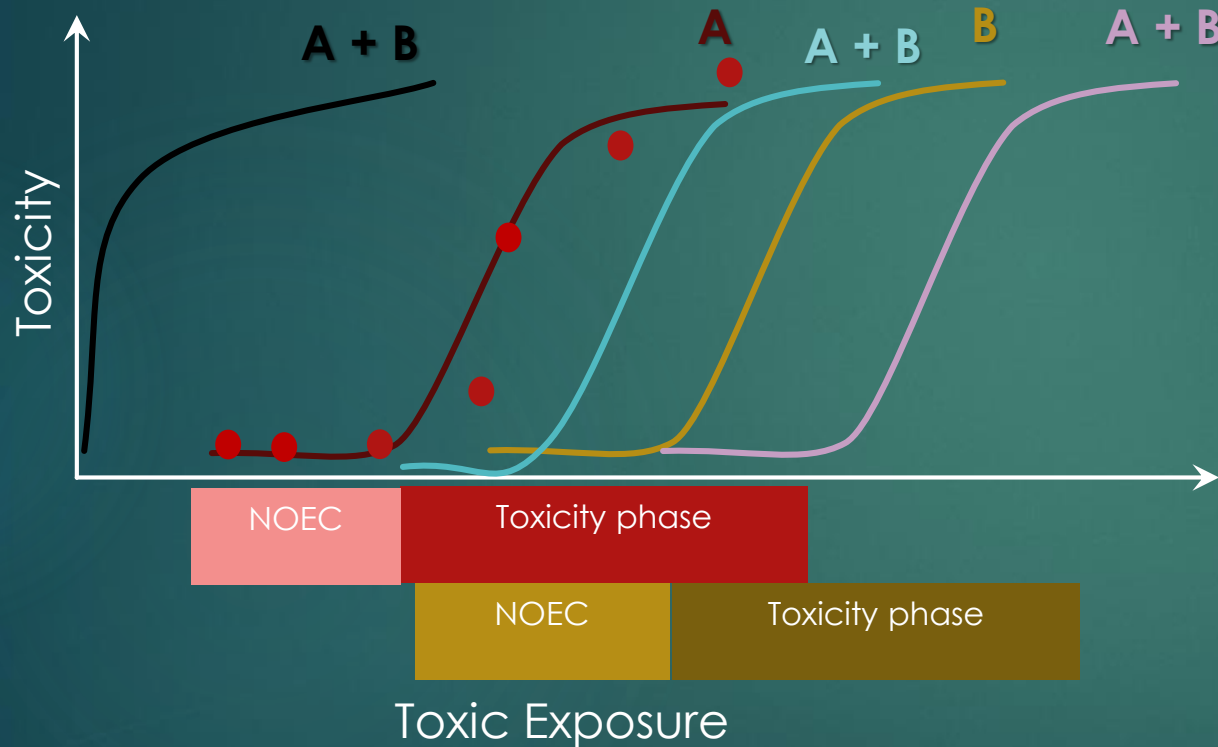
Toxic Exposure

Main types of interaction of toxicity

Additive effects

Exposure **A** ✚ **B** ═ Effect **A** ✚ Effect **B**

Antagonist effects

Exposure **A** ✚ **B** ═ Effect **A** ➖ Effect **B**

Synergism effects

Exposure **A** ✚ **B** ═ Effect **A** ✖ Effect **B**

Student activity (group): Discuss which shape to expect for the toxicity of simultaneous exposure to A & B?

Would you expect microplastics to act as single contaminant or as a mixture of contaminants?

Lecturer: Abel Machado

Summary: Measuring toxicity

A cause-consequence inference tool that controls exposure and endpoint to obtain accurate and precise dose-response estimates

Multiple purposes

Multiple audiences, common requirements

Multiple biological levels
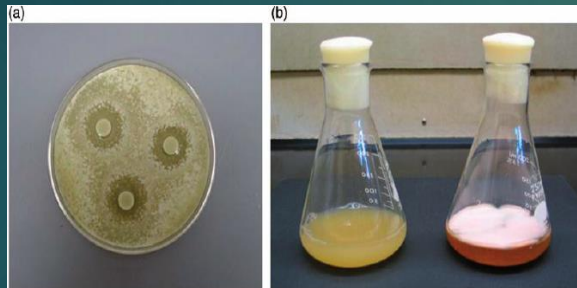

Multiple response to estimate

Lecturer: Abel Machado

Thanks

HOW COULD WE OBTAIN RELEVANT ECOTOXICOLOGICAL INFORMATION FROM OUR TOXICITY TESTS?

Terrestrial model	Animal model	Primary Producer model	Primary Producer model
Filamentous fungi	Zooplankton community	Microalgae	Terrestrial plant

TOMORROW WE WOULD OPTIMIZE THE TOXICITY TESTS. AS THERE WILL BE NO TIME FOR IT LET'S:

1- GET SOME RESEARCH DONE ON THE ECOTOXICOLOGICAL MODEL

2- DESIGN THE EXPOSURE PROTOCOLS AND THE CONCENTRATIONS YOUR GROUP WILL TO USE