

Environmental Toxicity Testing

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Toxicity Measures

EC ₅₀	Effective Concentration for 50% of a population
LD ₅₀	Lethal Dose for 50% of a population
LC ₅₀	Lethal Concentration for 50% of a population
NEL	No Effect Level
NOEL	No Observable Effect Level
NOAEL	No Observable Adverse Effect Level

Human Drug Toxicity Testing

Test species: Rats
 Mice
 Dogs
 Rabbits
 Isolated cells

- ↪ Extrapolate to humans.
- ↪ Are rats similar enough to humans?
- ↪ Array of tests from different mammals.

Environmental Toxicity Testing

10^7 animal/plant species

How do we decide which
to use for testing?

TROPHIC LEVEL

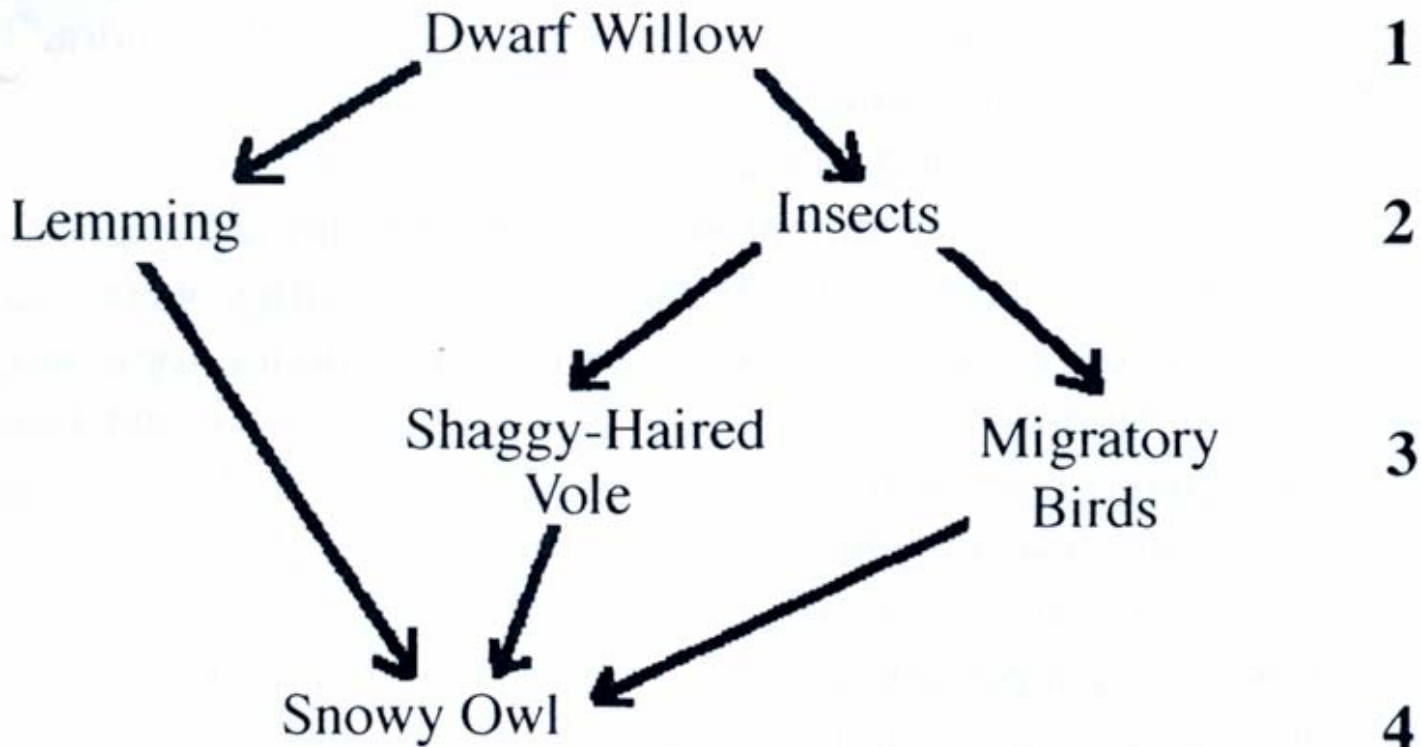


Figure 2.3 Complex food web showing the trophic levels.

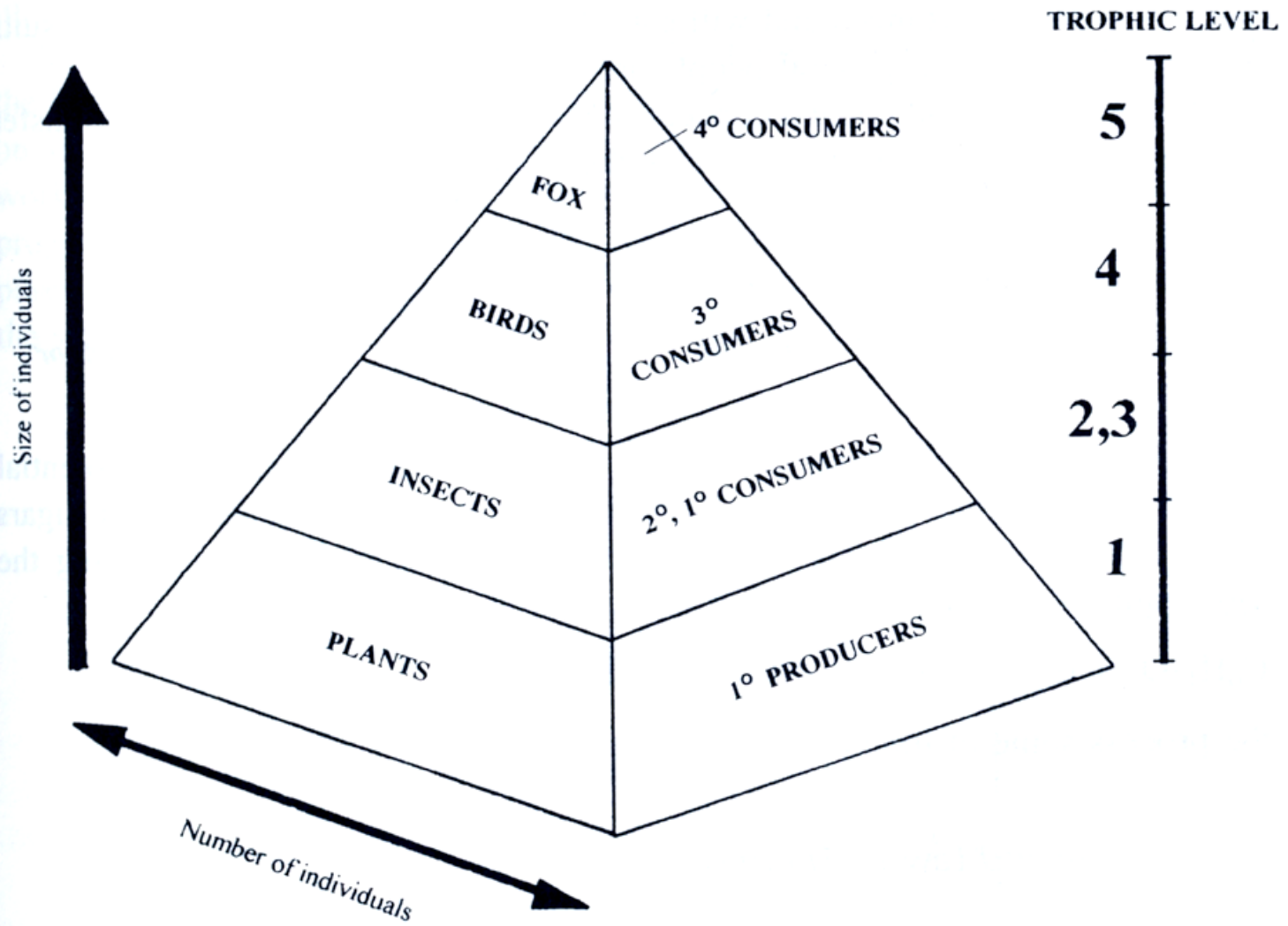


Figure 2.1 Pyramid representation of the trophic levels and their interactions.

Table 2.2 Food chain concentration of DDT in an east coast estuary in the USA

	Diet	DDT residues (parts per million)*
Water	N/A	0.00005
Plankton	N/A	0.04
Sheepshead minnow	Plankton	0.94
Pickeral	Predatory fish	1.33
Heron	Small fish	3.57
Herring gull	Scavenger	6.00
Osprey (eggs)	Larger fish	13.8
Merganser	Fish	22.8
Cormorant	Larger fish	26.4

Data from Woodwell, G.M., Worster, C.F.J. and Isaacson, P.A. (1967), *Science*, **156**, 821.

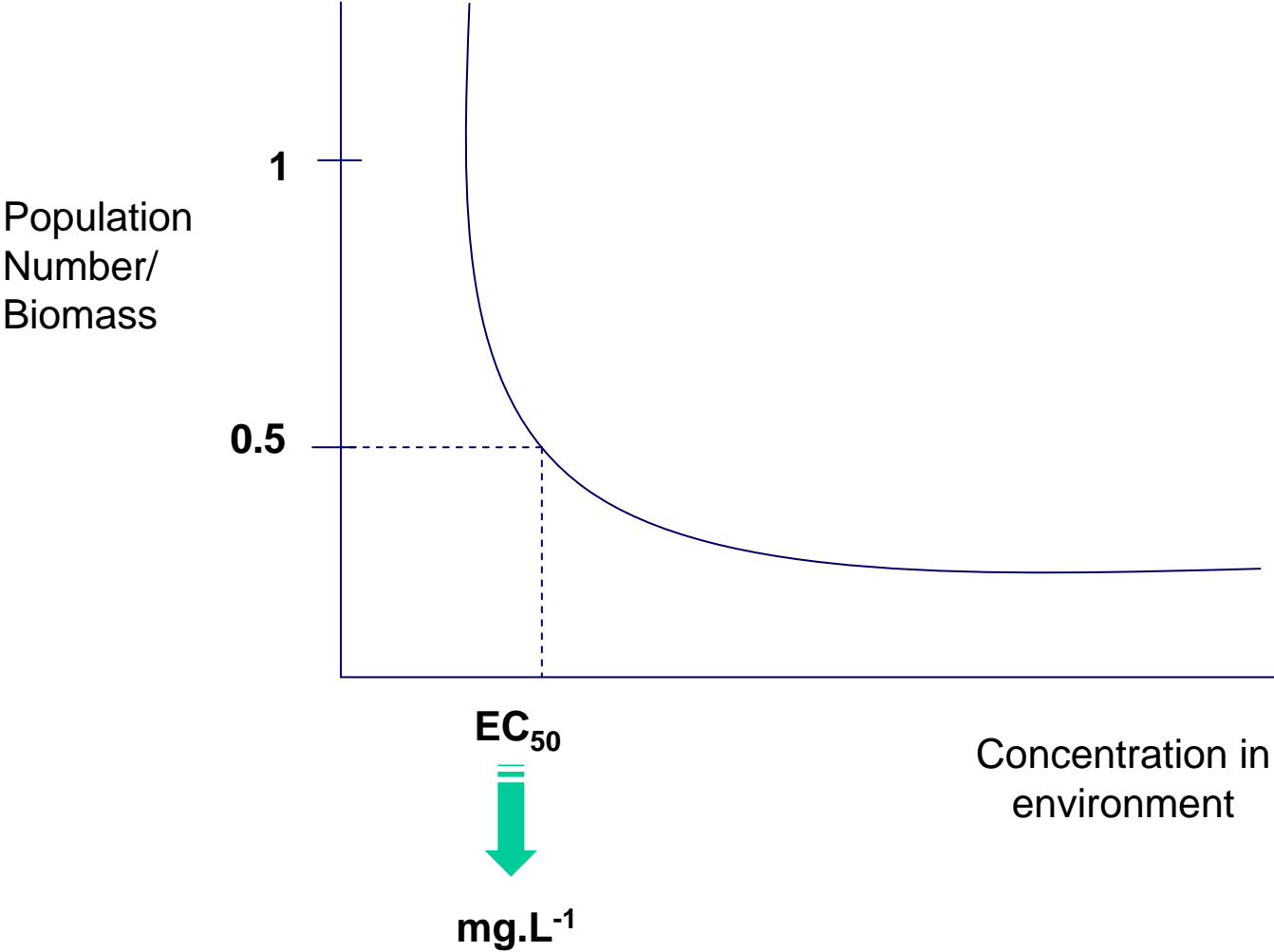
* Parts per million = mg.kg^{-1} or mg.dm^{-3} .

Table 2. Trophic levels showing the commonly used representatives in ecotoxicity testing.

Trophic level	Description	Example	Species generally used in testing
1	Primary producer	Algae	Blue green algae
2	Primary consumers	Daphnia	<i>Daphnia magna</i>
3	Secondary consumers (carnivores)	Water spider	No defined species
4	Tertiary consumers (carnivores)	Fish	Trout/blue gilled sun fish
5	Quaternary consumers (carnivores)	Birds of prey	Quail*

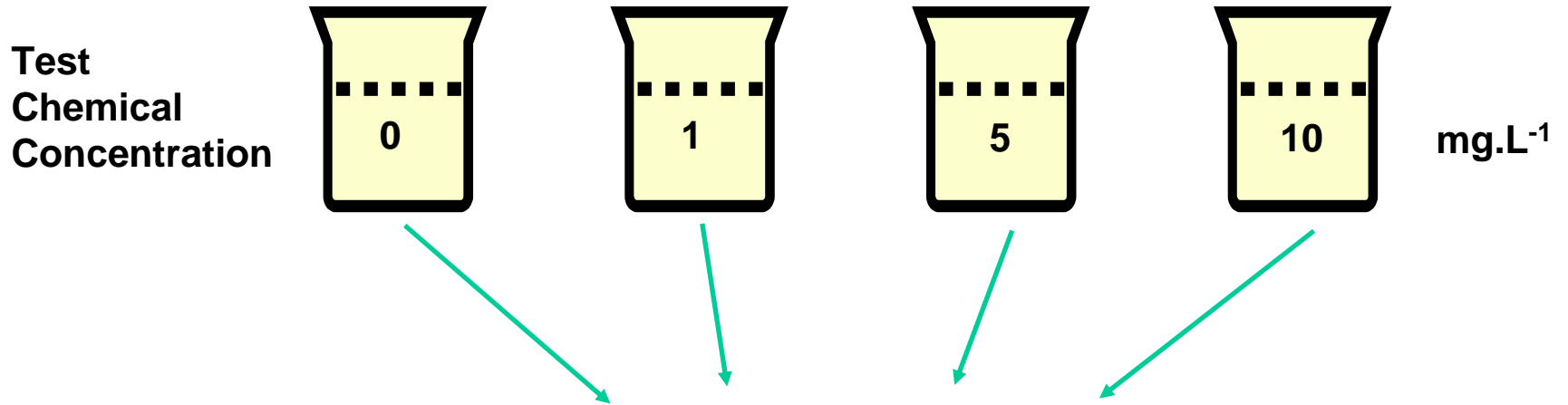
* Not a typical level 5 consumer but used to represent the type because of ease of keeping; however this animal does represent a human food species which is another important consideration.

EC₅₀



EC₅₀ Determination

Eg: chlorella sp.



Biomass 1

0.5

EC₅₀

Test Chemical Concentration

Hansch Coefficient

Octanol/Water partition coefficient

$$\text{Lg } P_{ow} = \frac{[X]_{\text{octanol}}}{[X]_{\text{water}}}$$

X = test chemical

Table 6.1 Log P_{ow} values for a selection of well-known pesticides

Pesticide	Log P_{ow}
DDT	6.2
Cypermethrin	6.3
Tributyltin oxide (TBTO)	3.2–3.8 ^a
Atrazine	2.6

^a This is the range of values for TBTO compounds generally.

It is clear that pesticides which are known to cause chronic environmental harm have values very much greater than 3. Even though cypermethrin has a value greater than 3 it is rapidly hydrolysed on contact with water and so does not persist.

Structure Activity Relationships

SAR

Similar molecular structures have similar toxicity profiles

An example of the relationship between molecular structure and toxicity

Benzidine is one of the most carcinogenic substances known, indeed its use in the UK is banned. It is a planar molecule with two aromatic amino groups.



This molecular planarity facilitates intercollation into DNA and the positions of the amino groups possibly allow a specific interaction with a DNA base (probably guanine) which results in irreversible DNA damage and eventually carcinogenesis. Benzidine is a genotoxic carcinogen.

Based on this philosophy one might predict aniline to be a potent carcinogen too.



However, it is not. The SAR for aromatic amino compound carcinogenesis therefore requires a planar hydrophobic aromatic region of significant size (eg. two benzene rings) plus one, or perhaps two, amino groups.

We can test this predictive hypothesis using 2,4'-biphenyldiamine (2,4-BD).

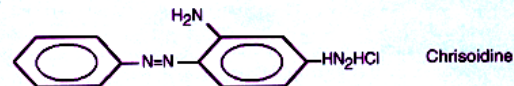


Wrong! 2,4-BD is not a carcinogen. Our hypothesis must be modified: perhaps the amino groups have to be in the 4-position. This can be tested using biphenylamine (BPA).

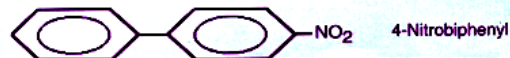


Correct! BPN is carcinogenic, but not as potent a carcinogen as benzidine.

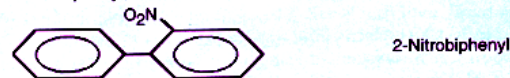
It appears that if a non-4-position amino group is present that this prevents a planar aromatic amino group from being carcinogenic. This is an important predictive property and therefore the hypothesis must be tested further. The planar aromatic amino dye, chrysoidine, proves the point nicely because it is not carcinogenic.



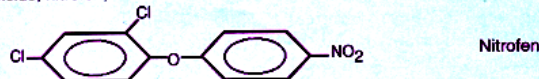
We are now beginning to build a good predictive picture in relation to carcinogenicity and planar aromatic amines. This line of reasoning can be continued to include other chemical moieties which have 'similar' properties to the amino group (eg. the nitro group). Indeed 4-nitrobiphenyl is carcinogenic,



whereas 2-nitrobiphenyl, ie,



is not. So the same rules seem to apply. If the rules are applied to the herbicide, nitrofen,



the predictive system developed thus far would alert one to nitrofen being a potential carcinogen. Indeed the IACR categorise nitrofen as 'reasonably anticipated to be a carcinogenic'. The system therefore works!