Valutazione del rischio chimico

CdL Magistrale Interateneo in
Scienze e Tecnologie per l'Ambiente e il Territorio
Università di Udine e Università di Trieste

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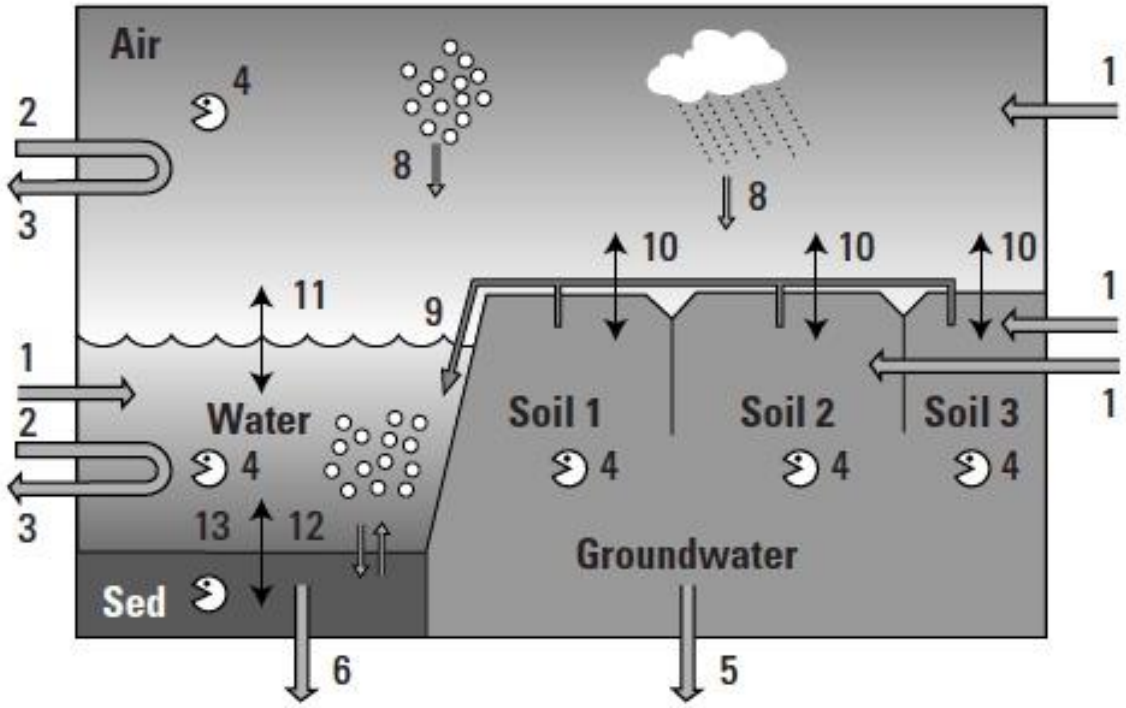

Figure 4.11. Diagram of a multimedia mass balance model concept. 1 = Emission, 2 = Import, 3 = Export, 4 = Degradation, 5 = Leaching, 6 = Burial, 7 = Wet deposition, 8 = Dry aerosol deposition, 9 = Run-off, 10, 11 = Gas absorption and volatilization, 12 = Sedimentation and resuspension, 13 = Sorption and desorption. From [61]

I processi di degradazione abiotica e biologica

BIODEGRADAZIONE

La degradazione microbica ha un ruolo chiave nella rimozione delle sostanze chimiche di sintesi negli *ambienti acquatici e terrestri*.

Inizialmente era vista come aspetto indesiderato, associato a ridotta durata di prodotti dell'industria (perseguita "persistenza")

Successivamente si è realizzato che biodegradazione troppo lenta può provocare accumulo nei comparti ambientali e negli organismi / avvelenamento primario e secondario nelle reti trofiche / compromissione delle risorse idriche.

Impatto estetico **visibile** (plastiche, schiume)

Rischio ecologico interazione con (tensioattivi, PCB, DDT, aldrin ect.)

Pericolo per la salute umana (diossine e pesticidi nel cibo e nelle acque potabili)

ELSEVIER

Marine Pollution Bulletin

Volume 128, March 2018, Pages 89-96

Ingestion of microplastics and natural fibres in *Sardina pilchardus* (Walbaum, 1792) and *Engraulis encrasicolus* (Linnaeus, 1758) along the Spanish Mediterranean coast

Montserrat Compa, Ana Ventero, Magdalena Iglesias, Salud Deudero

Show more

https://doi.org/10.1016/j.marpolbul.2018.01.009

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Highlights

- Fifteen percent of sampled European pilchards and European anchovies ingested microplastics and natural fibres.
- Condition index (Fulton's K) influences the ingestion of microplastics and natural fibres in the sampled European pilchard.

ELSEVIER

Chemosphere

Volume 71, Issue 6, April 2008, Pages 1005-1018

Review

Microbial degradation of chlorinated dioxins

Jim A. Field, Reyes Sierra-Alvarez

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https://doi.org/10.1016/j.chemosphere.2007.10.039

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ENVIRONMENTAL Science & Technology

Viewpoint

Cite This: Environ. Sci. Technol. 2017, 51, 12058-12060

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Biodegradability of Plastics: Challenges and Misconceptions

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SCIENTIFIC OPINION NON-PEER REVIEWED

ABSTRACT: Plastics are one of the most widely used materials and, in most cases, they are designed to have long life times. Thus, plastics contain a complex blend of stabilizers that prevent them from degrading too quickly. Unfortunately, many of the most advantageous properties of plastics such as their chemical, physical and biological inertness and durability present challenges when plastic is released into the environment. Common plastics such as polyethylene (PE), polypropylene (PP), polystyrene (PS), and polyethylene terephthalate (PET) are extremely persistent in the environment, where they undergo very slow fragmentation (projected to take centuries) into small particles through photo-, physical, and biological degradation processes[1]. The fragmentation of the material into increasingly smaller pieces is an unavoidable stage of the degradation process. Ultimately, plastic materials degrade to micron-sized particles (microplastics), which are persistent in the environment and present a potential source of harm for organisms.

RESEARCH Review

Dichlorodiphenyltrichloroethane (DDT): Ubiquity, Persistence, and Risks

Vladimir Turusov,[1] Valery Rakitsky,[2] and Lorenzo Tomatis[3]

[1]N.N. Blokhin Russian Cancer Research Centre, Moscow, Russian Federation; [2]F.F. Erisman Federal Centre of Hygiene, Moscow Region, Russian Federation; [3]Aurisina (Trieste), Italy

Due to uncontrolled use for several decades, dichlorodiphenyltrichloroethane (DDT), probably the best known and most useful insecticide in the world, has damaged wildlife and might have negative effects on human health. This review gives a brief history of the use of DDT in various countries and presents the results of epidemiologic and experimental studies of carcinogenesis. Even though its use has been prohibited in most countries for ecologic considerations, mainly because of its negative impact on wildlife, it is still used in some developing countries for essential public health purposes, and it is still produced for export in at least three countries. Due to its stability and its capacity to accumulate in adipose tissue, it is found in human tissues, and there is now not a single living organism on the planet that does not contain DDT. The possible contribution of DDT to increasing the risks for cancers at various sites and its possible role as an endocrine disruptor deserve further investigation. Although there is convincing experimental evidence for the carcinogenicity of DDT and of its main metabolites DDE and DDD, epidemiologic studies have provided contrasting or inconclusive, although prevailingly negative, results. The presence and persistence of DDT and its metabolites worldwide are still problems of great relevance to public health. Efficient pesticides that do not have the negative properties of DDT, together with the development of alternative methods to fight malaria, should be sought with the goal of completely banning DDT. *Key words:* carcinogenesis, DDT, estrogenic effects, wildlife. *Environ Health Perspect* 110:125–128 (2002). [Online 10 January 2002] *http://ehpnet1.niehs.nih.gov/docs/2002/110p125-128turusov/abstract.html*

DDT in agriculture were banned (*11*), but its use for public health purposes (destruction of insects such as mosquitoes, malarial plasmodia, fleas, lice, ticks) was still permitted. In March 1989, DDT was also banned for medical-disinfecting purposes. Its use, in limited volumes, was permitted for medical purposes after epidemiologic alerts and only with the permission of the state administration for sanitary matters.

In other countries, most uses of DDT were banned in 1972 or shortly thereafter because of its negative impact on wildlife (*12*), not because of the evidence for carcinogenicity in long-term tests in rodents. Epidemiologic studies that showed no significant long-term adverse effects were held to be more relevant than the experimental evidence of dose-related induction of liver tumors in rodents, although studies were carried out on

Environmental Health Perspectives, 110|2|2002
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1240724/pdf/ehp0110-000125.pdf

BIODEGRADAZIONE

- Trasformazione da *composto genitore (parent compound)* a altro composto organico è nota come *biodegradazione "primaria"*

- Biodegradazione in ambienti aerobici -> prodotti finali CO_2 e H_2O (*mineralizzazione*)

In ambienti aerobici la sopravvivenza dei microorganismi eterotrofi è spesso condizionata dalla disponibilità di fonti di carbonio.

In ambienti anaerobici i processi di degradazione microbica sono in genere più lenti e possono non portare alla mineralizzazione. In comparti metanogeni si intende per mineralizzazione la conversione a prodotti finali con un solo atomo di carbonio

L'organizzazione dei microorganismi eterotrofi è caratterizzata da versatilità catabolica (adattamento o acclimatamento)

Microflore in miscela - piuttosto che monocolture - degradano i *chemicals*

L'adattamento è un cambiamento nella comunità microbiologica eterotrofa che realizza cambiamenti metabolici (es. induzione enzimatica, cambiamenti di popolazione, trasferimento genetico, mutazione) e aumenta la velocità di biodegradazione di una specie chimica come risultato di una precedente esposizione al composto. L'apparato enzimatico consiste in enzimi coinvolti in cicli metabolici fondamentali (es. idrolisi) e enzimi adattivi o indotti. Questi enzimi consentono di batteri di usare composti organici (substrati) non adatti per l'uso immediato.

Fattori ambientali: aerobicità (sedimenti e suoli) è condizionata da rapporto tra velocità di consumo microbiologico di O_2 e velocità di diffusione O_2

Archives of Environmental Protection
Vol. 42 no. 4 pp. 3–11

PL ISSN 2083-4772
DOI 10.1515/aep-2016-0041

DE GRUYTER OPEN

Activity and functional diversity of microbial communities in long-term hydrocarbon and heavy metal contaminated soils

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Keywords: polycyclic aromatic hydrocarbons, heavy metals, microbial activity, functional diversity, Community Level Physiological Profiles.

Abstract: The impacts of long-term polycyclic aromatic hydrocarbons (PAHs) and heavy metal pollution on soil microbial communities functioning were studied in soils taken from an old coke plant. The concentrations of PAHs in the tested soils ranged from 171 to 2137 mg kg^{-1}. From the group of tested heavy metals, concentrations of lead were found to be the highest, ranging from 57 to 3478 mg kg^{-1}, while zinc concentrations varied from 247 to 704 mg kg^{-1} and nickel from 10 to 666 mg kg^{-1}. High dehydrogenase, acid and alkaline phosphatase activities were observed in the most contaminated soil. This may indicate bacterial adaptation to long-term heavy metal and hydrocarbon contamination. However, the Community Level Physiological Profiles (CLPPs) analysis showed that the microbial functional diversity was reduced and influenced to a higher extent by some metals (Pb, Ni), moisture and conductivity than by PAHs.

Kowalczyk, Agnieszka (2013) *Role of microbial adaptation in the biodegradation of chemical pollutants : extrapolation from laboratory to rivers.* PhD thesis, University of Warwick. http://wrap.warwick.ac.uk/58442/

Pollutant Effects on the Microbial Ecosystem

Tim Ford

Department of Environmental Health, Harvard School of Public Health, Boston, Massachusetts

Genetic diversity of a microbial community will inevitably be affected by environmental stress. However, our understanding of the implications of these effects is limited. Genetic exchange between natural microbial communities appears to be a common phenomenon, mediated by a number of microbial processes (conjugation, transformation, and transduction). These mechanisms of change are presumably adaptations to natural environmental perturbation, e.g., the low levels of antibiotics produced by other organisms. However, anthropogenic influences on the environment may be accelerating genetic change within microbiologic ecosystems, beyond these natural adaptation rates. This article highlights some of the perceived risks to ecosystem health and research questions that need to be addressed. — Environ Health Perspect 102(Suppl 12):45–48 (1994)

Key words: diversity, pathogens, plasmids, tolerance/resistance, virulence factors, antibiotic resistance factors

- *Batteri aerobi* usano O_2 sia come reagente per l'ossidazione dei composti organici che come accettore terminale degli elettroni (serve per la *dissimilazione* : conversione del composto organico - come sorgente energetica - in CO_2).
- *Batteri anaerobi facoltativi* usano l'O_2 ma hanno la possibilità di usare un altro accettore di elettroni se l'ambiente diviene anaerobico (es. batteri denitrificanti e solforiduttori)
- *Batteri anaerobi obbligati* : per essi O_2 è tossico

Table 3.10. Free energy of redox reactions in the saturated zone of soil. Calculations are based on data from [126,127].

Environment (electron acceptor)	-DG (kJ)	Relative to oxygen %	Reaction equation
Oxygen	472.5	100	$O_2 + CH_2O \rightarrow CO_2 + H_2O$
Nitrate	462.8	97.9	$4/5\ NO_3^- + 4/5\ H^+ + CH_2O \rightarrow 2/5\ N_2 + CO_2 + 7/5\ H_2O$
Nitrate/nitrite	332.8	70.4	$2\ NO_3^- + CH_2O \rightarrow 2\ NO_2^- + CO_2 + H_2O$
Pyrolusite	364.2	77.1	$2\ MnO_2 + 4\ H^+ + CH_2O \rightarrow 2\ Mn^{2+}\ CO_2 + 3\ H_2O$
Manganite	320.9	67.9	$4\ MnOOH + 8\ H^+ + CH_2O \rightarrow 4\ Mn^{2+} + CO_2 + 7\ H_2O$
Hausmannite	330.6	70.0	$2\ Mn_3O_4 + 12\ H^+ + CH_2O \rightarrow 6\ Mn^{2+} + CO_2 + 7\ H_2O$
Hematite	60.0	12.7	$2\ Fe_2O_3 + 8\ H^+ + CH_2O \rightarrow 4\ Fe^{2+} + CO_2 + 5\ H_2O$
Magnetite	27.1	5.7	$2\ Fe_3O_4 + 12\ H^+ + CH_2O \rightarrow 6\ Fe^{2+} + CO_2 + 7\ H_2O$
Sulphate	98.1	20.8	$1/2\ SO_4^{2-} + H^+ + CH_2O \rightarrow 1/2\ H_2S + CO_2 + H_2O$
H2 production	26.0	5.5	$H_2O + CH_2O \rightarrow 2\ H_2 + CO_2$
Methanogenic	91.4	19.3	$CH_2O \rightarrow 1/2\ CH_4 + 1/2\ CO_2$

- Energia guadagnata da batteri con ossidazione di un atomo di C per diversi elettron accettori è molto diversa-> diversa velocità di degradazione
- Se biodegradazione di specie chimiche di sintesi non sufficiente per generare crescita batterica si può avere cometabolismo

Biodegradazione aerobica **e pathways metabolici**

Chemicals come nutrienti per batteri con varietà di meccanismi biochimici.

Per reazioni senza e con nitrificazione si ha:

$$C_cH_hO_oN_nNa_{na}P_pS_sX_x + (c + 1/4\,(h - x - 3n) + na/4 + 5p/4 + 3s/2)\,O_2 + (3p/2 + s)\,H_2O \rightarrow cCO_2 + 1/2\,(h - x - 3n)\,H_2O + nNH_3 + na/2\,Na_2O + pH_3PO_4 + sH_2SO_4 + xHX \quad (3.65)$$

$$C_cH_hO_oN_nNa_{na}P_pS_sX_x + (c + 1/4\,(h - x) + 5n/4 + na/4 + 5p/4 + 3s/2)\,O_2 + (n/2 + 3p/2 + s)\,H_2O \rightarrow cCO_2 + 1/2\,(h - x)\,H_2O + nHNO_3 + na/2\,Na_2O + pH_3PO_4 + sH_2SO_4 + xHX \quad (3.66)$$

Se sostanza è completamente mineralizzata, sono calcolabili

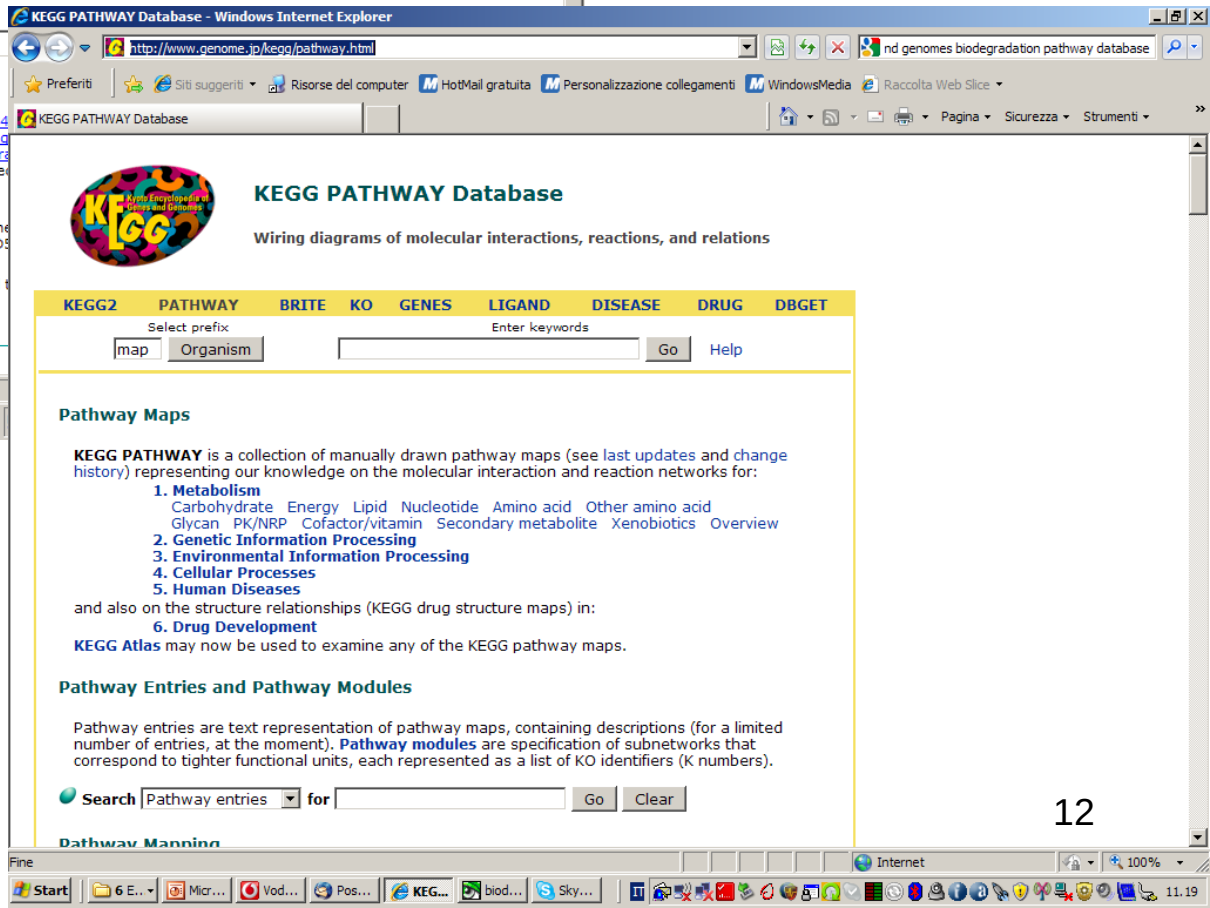
richiesta di ossigeno teorica *ThOD* e

produzione di diossido di carbonio teorica $ThCO_2$

$$ThOD\ (mg\ O_2 / mg\ subst.) = (MW\ Oxygen / MW\ subst.) \times (c + 1/4\,(h - x - 3n) + na/4 + 5p/4 + 3s/2) \quad (3.67)$$

$$ThOD\ (mg\ O_2 / mg\ subst.) = (MW\ Oxygen / MW\ subst.) \times (c + 1/4\,(h - x) + 5n/4 + na/4 + 5p/4 + 3s/2) \quad (3.68)$$

$$ThCO_2\ (mg\ CO_2 / mg\ subst.) = (MW\ Carbondioxide / MW\ subst.) \times c$$



Pathways di degradazione microbica

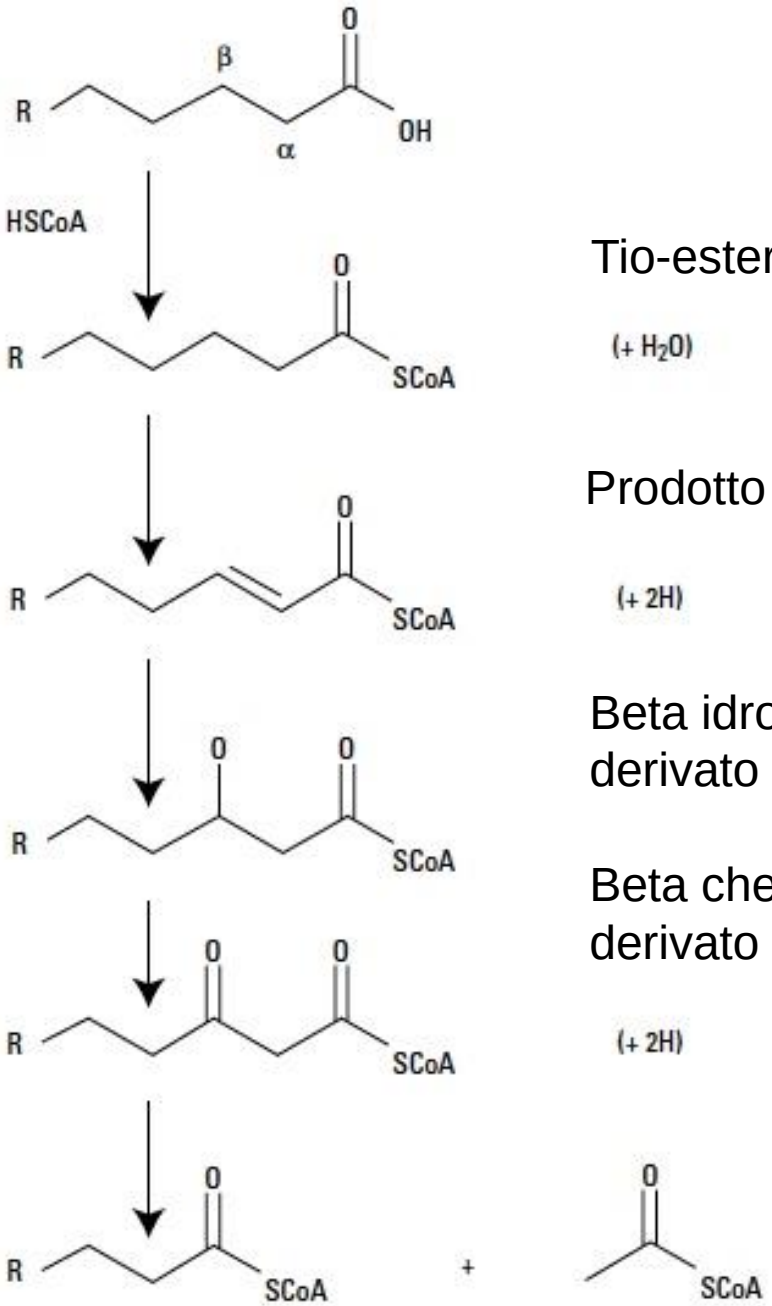
Biodegradazione aerobica

- Ossidazione **omega** (metile terminale -> alcol -> acido carbossilico , richiede *ossigenasi*)
- Ossidazione **beta** a un doppio legame di un acido grasso
- Ossidazione **aromatica**

Ossidazione omega

http://en.wikipedia.org/wiki/Omega_oxidation

Ossidazione beta



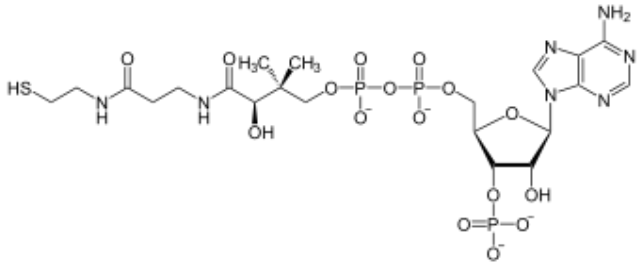
Tio-estere

Prodotto insaturo

Beta idrossi-derivato

Beta cheto-derivato

Figure 3.34. β-oxidation of aliphatic hydrocarbons by bacteria. (H)SCoA = Coenzyme A.



Ossidazione aromatica

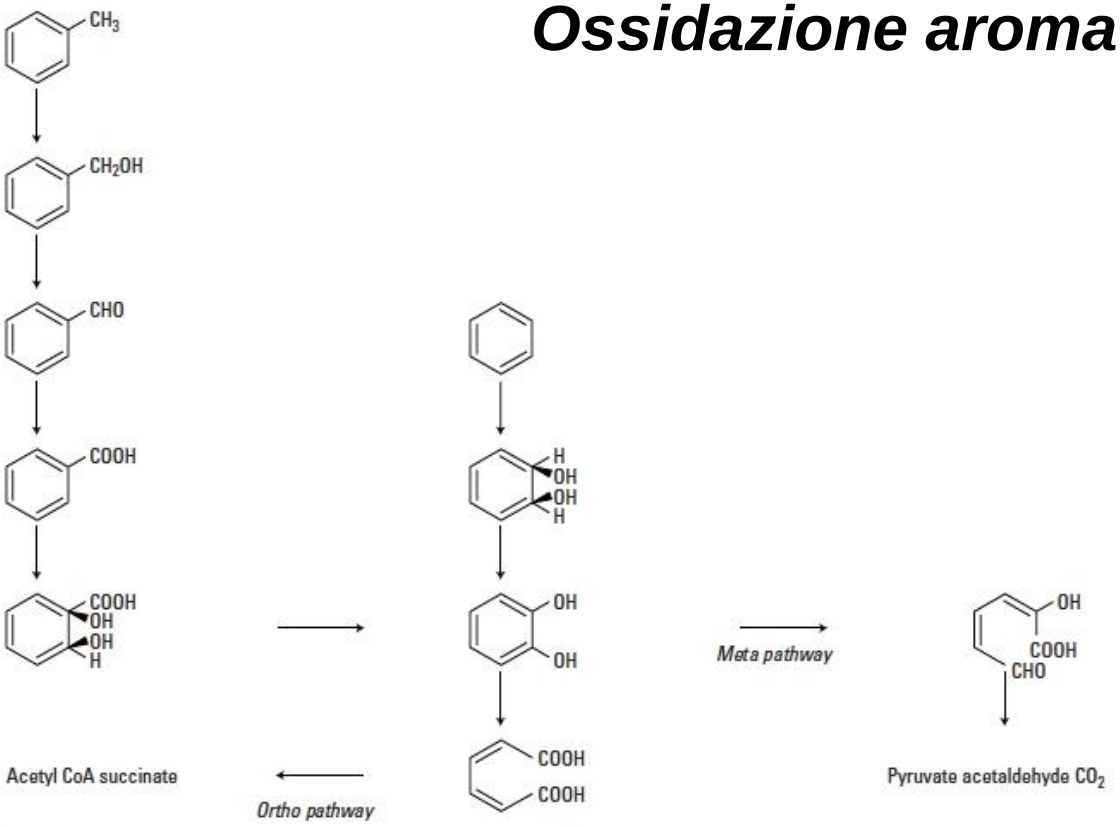
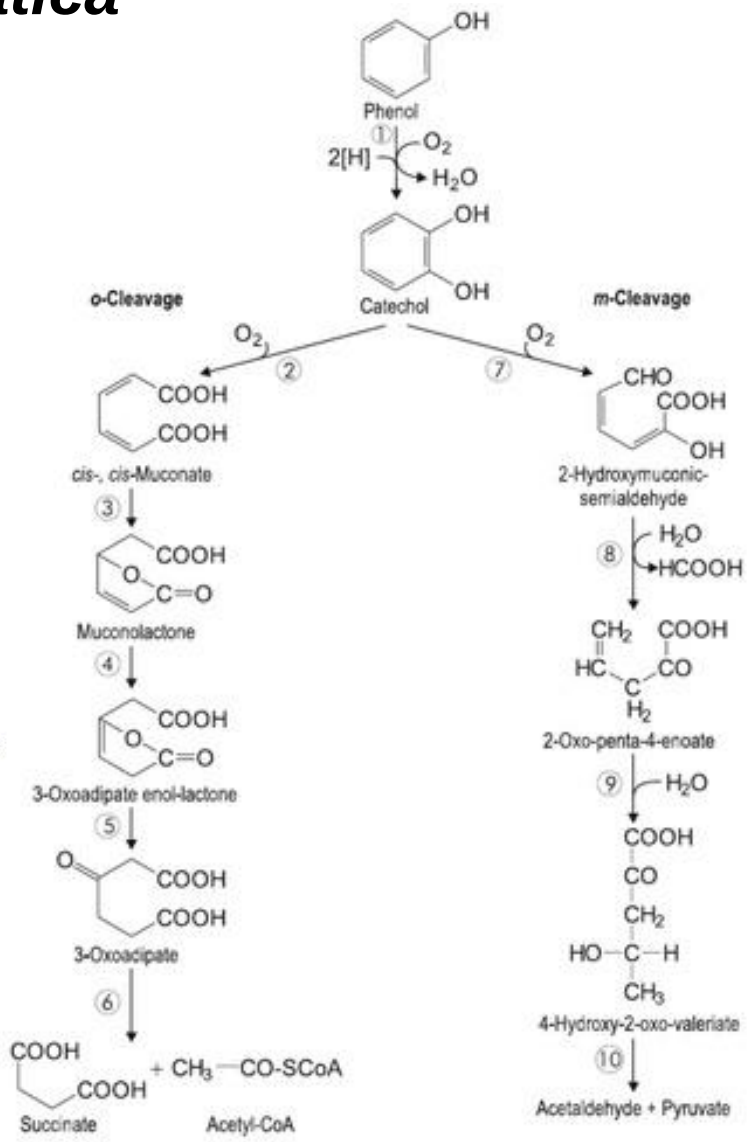


Figure 3.35. Aromatic oxidation by bacteria after catechol formation. Left *ortho* and right, *meta* fission.



Environmental Biotechnology: Concepts and Applications
a cura di Hans-Joachim Jördening,Josef Winter

Degradazioni anaerobiche

Assenza di O_2 quale accettore terminale di elettroni

Ambienti con riduzione di Nitrati, di Ferro (FeIII), di Manganese (Mn IV), di Solfati e perfino CO2

Nella metanogenesi si ha mineralizzazione con conversione in prodotti che contengono un atomo di carbonio

$$C_cH_hO_o + (c - h/4 - o/2)\, H_2O \rightarrow (c/2 + h/8 + o/4)\, CH_4 + (c/2 - h/8 + o/4)\, CO_2$$

Rilevanti per dealogenazione riduttiva nei sedimenti
MTBE biodegrada più favorevolmente in condizioni anaerobiche che aerobiche
Dealogenazione riduttiva

Esistono protocolli OECD per valutare la biodegradabilità in ambiente metanogeno

Table 3.12 Ready biodegradability tests (RBT) and inherent biodegradability tests (IBT) according to the OECD. Population densities are in colony forming units (CFU) per ml. From [133,141].

OECD test guideline	Summary parameter	Population density (CFU/ml)
Ready biodegradability		
301E: Modified OECD screening test	DOC	$(0.5 - 2.5) \times 10^2$
301B: CO_2 evolution	CO_2	$(2 - 10) \times 10^5$
301F: Manometric respirometry test	O_2	$(2 - 10) \times 10^5$
301A: DOC Die-away test	DOC	$(2 - 10) \times 10^5$
301D: Closed bottle test	O_2	$(0.5 - 2.5) \times 10^3$
301C: Modified MITI(I) test	O_2	$(2 - 10) \times 10^5$
306: Biodegradability in Seawater	DOC	
Inherent biodegradability		
302B: Zahn-Wellens test	DOC	$(0.7 - 3) \times 10^7$
302A: Modified SCAS test	DOC	$(2 - 10) \times 10^7$
302C: Modified MITI(II) test	O_2	$(0.7 - 3) \times 10^6$
Simulation tests		
303A: Activated Sludge Units	DOC	
303B: Biofilms	DOC	
304A: Inherent Biodegradability in Soil	$^{14}CO_2$	
307: Aerobic and Anaerobic Transformation in Soil	$^{14}CO_2 / CO_2$	
308: Aerobic and Anaerobic Transformation in Aquatic Sediment Systems	$^{14}CO_2 / CO_2$	
309: Aerobic Mineralization in Surface Water	$^{14}CO_2 / CO_2$	

Table 3.11. Influence of molecular structure on the biodegradability of chemicals in the aerobic environment.

Type of compounds or substituents	More biodegradable	Less biodegradable
Hydrocarbons	linear alkanes > C_{12}	linear alkanes < C_{12}
	alkanes with not too high molecular weight	high molecular weight alkanes
	linear chain	branched chain
	-C-C-C-	-C-O-C-
	aliphatic	aromatic
	mono- and bicyclic aromatic	polycyclic aromatic
Aliphatic chlorine	Cl more than 6 carbons from terminal carbon	Cl at 6 or less carbon atoms from terminal C
Substituents to an aromatic ring	-OH	-F
	$-CO_2H$	-Cl
	$-NH_2$	$-NO_2$
	$-OCH_3$	$-CF_3$

Una molecola persistente:

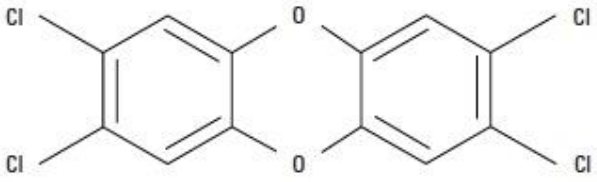


Figure 3.36. Molecular structure of 2,3,7,8-tetrachloro-*p*-dioxin (TCDD).

Table 3.13 Ready biodegradability tests (RBT) and inherent biodegradability tests (IBT) according to the OECD. Population densities are in colony forming units (CFU) per ml. From [61,62]

Type of test	Summary parameter	Population density (CFU/ml)
Ready biodegradability test [61]		
Modified OECD screening test	DOC	$(0.5 - 2.5)\times10^{2}$
CO_2 evolution	CO_2	$(2 - 10)\times10^{5}$
Manometric respirometry	O_2	$(2 - 10)\times10^{5}$
DOC die-away	DOC	$(2 - 10)\times10^{5}$
Closed bottle	O_2	$(0.5 - 2.5)\times10^{3}$
MITI(I)	O_2	$(2 - 10)\times10^{5}$
Inherent biodegradability [61]		
Zahn-Wellens test	DOC	$(0.7 - 3)\times10^{7}$
SCAS test	DOC	$(2 - 10)\times10^{7}$
MITI(II)	O_2	$(0.7 - 3)\times10^{6}$

BIOTRASFORMAZIONI

Le specie chimiche nell'ambiente entrano in contatto con e sono assorbite da organismi

Se le concentrazioni negli organismi raggiungono valori critici ci possono essere alterazioni della normale fisiologia.

Le specie chimiche possono essere eliminate per escrezione nella forma originale o modificandone la struttura

- Microorganismi -> *biodegradazione*
- Altri organismi -> ***biotrasformazioni***

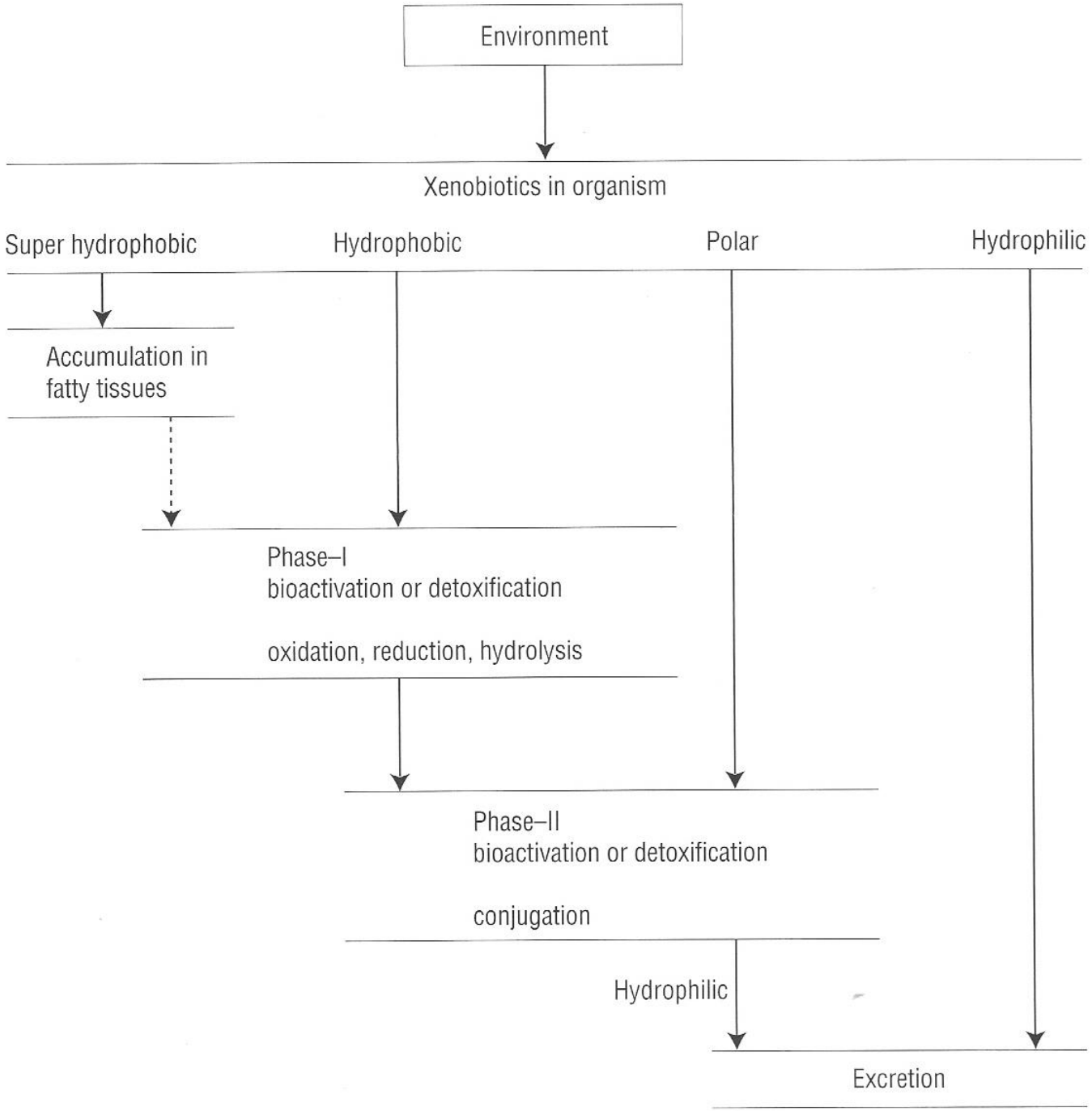
Enzimi (catalizzatori biologici)

Per lipidi / proteine /carboidrati -> metabolismo

Per xenobiotici -> biotrasformazione

Bioattivazione o Detossificazione

Prodotti meno idrofobici dei composti genitori



3.38. General pathways of biotransformation of xenobiotics in living organisms.

Reazioni di Fase I : *non sintetiche* (idrolisi, ossidazioni e riduzioni)

Reazioni di Fase II : *sintetiche* (coniugazioni)

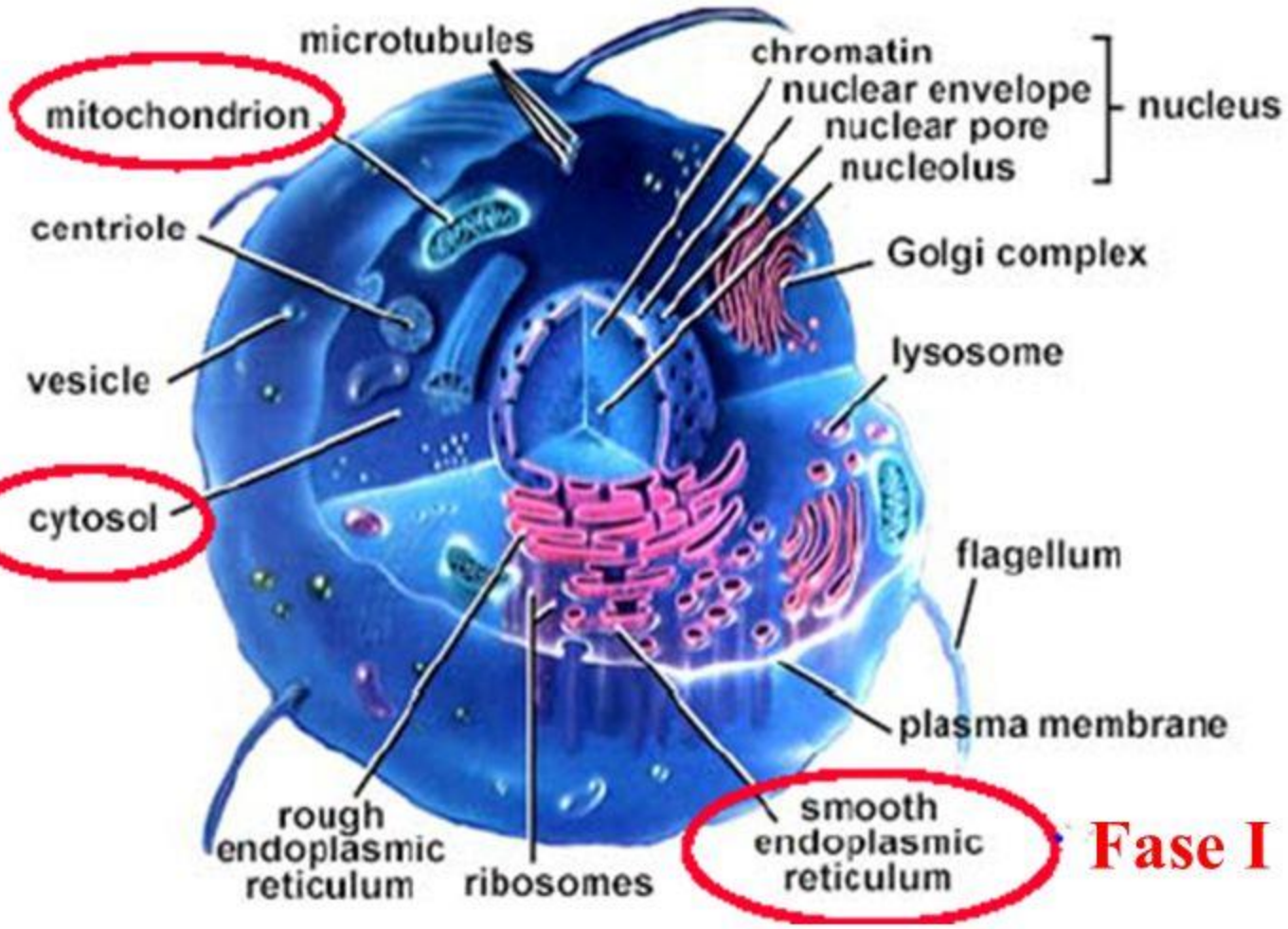
Reazioni di Fase I Introducono nelle specie chimiche gruppi –OH, -COOH, -NH_2, che generano specie reattive che possono esser facilmente coniugate (Fase II) ed escrete

Tipi di reazione di biotrasformazione

Table 3.14 The most important enzyme systems which metabolize pesticides [63]

Enzyme system	Location	Compounds metabolized
Phase-I reactions:		
Mixed function oxidases	Microsomes, notably from vertebrate liver and insect fat body	Many liposoluble pesticides
Phosphatases	Present in nearly all tissues and subcellular fractions of species	Organophosphorus insecticides and "nerve gases"
Carboxyesterases	In most tissues of insects and vertebrates	Malathion and malaoxon
Epoxide hydroxilase	Microsomes, particularly in the mammalian liver	Dieldrin, heptachlor and arene epoxides
DDT dehydrochlorinase	Virtually all insects and vertebrates	*p,p'*-DDT and *p,p'*-DDD
Phase-II reactions:		
Glucuronyl transferases	Mainly in microsomes; widespread in vertebrates other than fish and insects	Compounds with labile hydrogen, including hydroxylated metabolites
Glutathione-S-transferases	70,000 g supernatants of vertebrates livers and also insects	Chlorinated compounds, e.g. γ-HCH; also some epoxides

Fase I

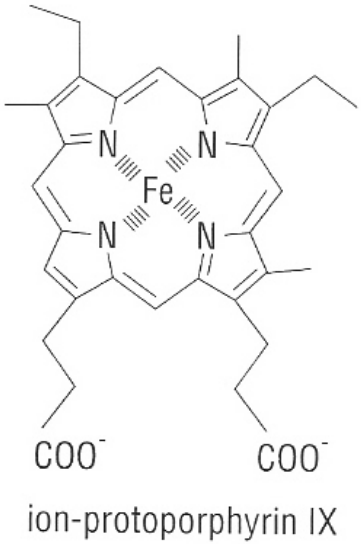


Fase II

Fase I

Gli enzimi della fase I predominano nel reticolo endoplasmatico liscio (microsomi), quelli della fase II nel citosol

Sistema enzimatico ***ossidasi a funzione mista*** (*Mixed Function Oxidase –MFO),* di cui il ***citocromo P450*** è parte, inserisce un atomo di O sul substrato e riduce l'altro atomo di O ad acqua



ion-protoporphyrin IX

Citocromo P450 superfamiglia enzimatica di emoproteine presente in tutti i domini dei viventi (sono note più di 7.700 distinte macromolecole di tipo CYP), appartenente alla sottoclasse enzimatica delle ossidasi a funzione mista (o monoossigenasi)

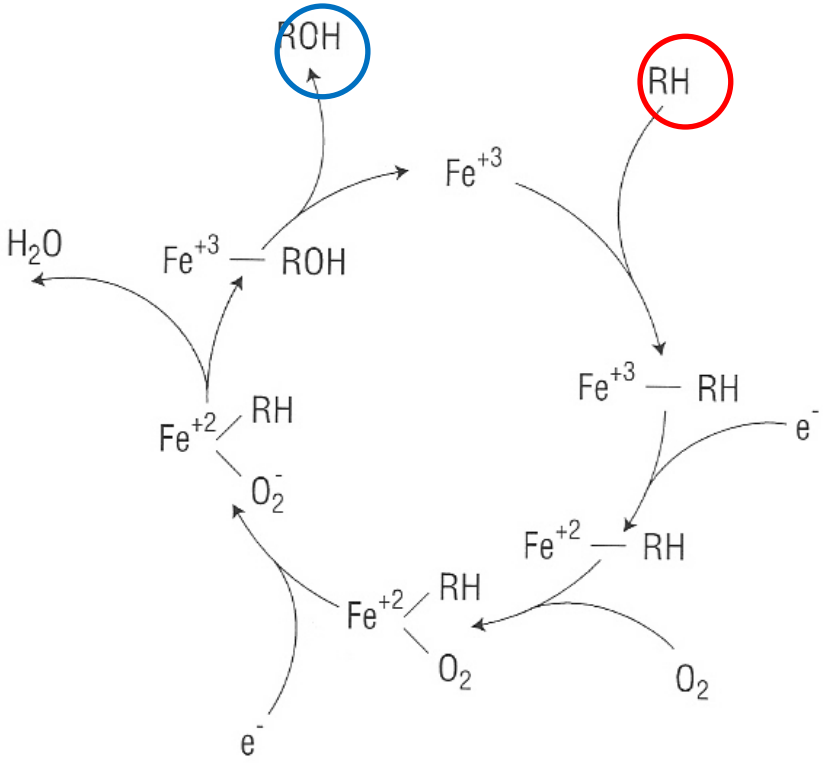


Figure 3.40. Mechanism of oxidation by cytochrome P-450.

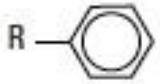
Widely distributed enzymes that carry out oxidation-reduction reactions in which one atom of the oxygen molecule is incorporated into the organic substrate; the other oxygen atom is reduced and combined with hydrogen ions to form water. They are also known as monooxygenases or hydroxylases. These reactions require two substrates as reductants for each of the two oxygen atoms. There are different classes of monooxygenases depending on the type of hydrogen-providing cosubstrate (COENZYMES) required in the mixed-function oxidation

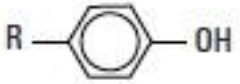
MFO

Le più comuni reazioni di biotrasformazione degli xenobiotici nel biota (continua)

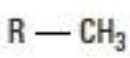
Oxidations

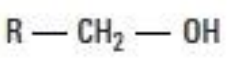
1. Aromatic hydroxylation



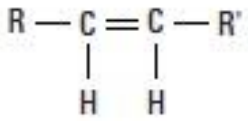


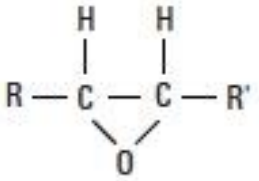
2. Aliphatic hydroxylation



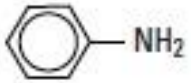


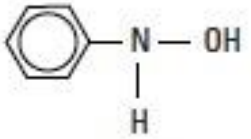
3. Epoxidation



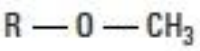


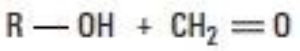
4. N-hydroxylation



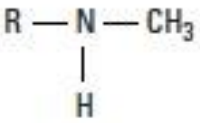


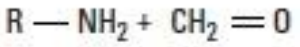
5. O-dealkylation



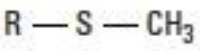


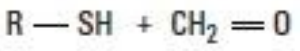
6. N-dealkylation



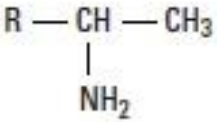


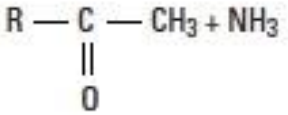
7. S-dealkylation





8. Deamination





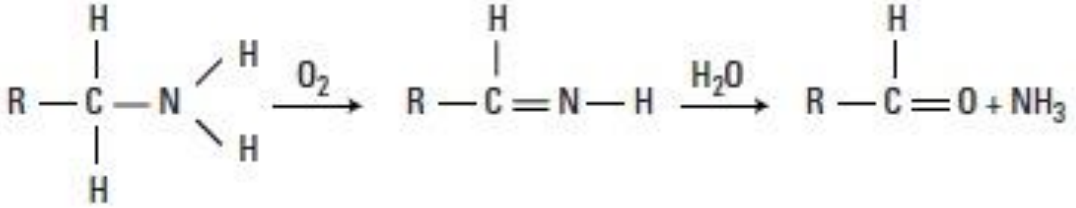
(continua) le più comuni reazioni di biotrasformazione degli xenobiotici nel biota

9. Sulphoxidation

10. Dehalogenation

11. Desulphuration

12. Monoamine and diamine oxidation

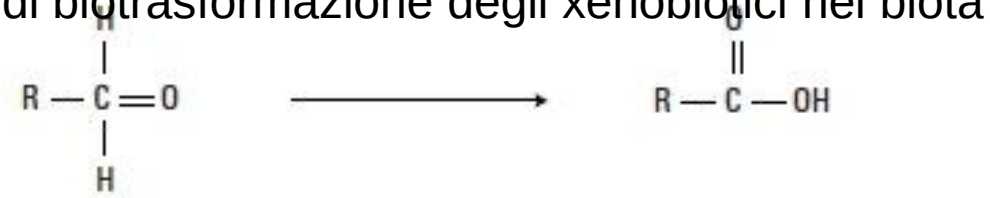


13. Alcohol dehydrogenation

(continua) le più comuni reazioni di biotrasformazione degli xenobiotici nel biota

Oxidations (continued)

14. Aldehyde dehydrogenation



Reductions

15. Azo reduction

16. Nitro reduction

17. Dehalogenation non-microsomal reduction

18. Aldehyde

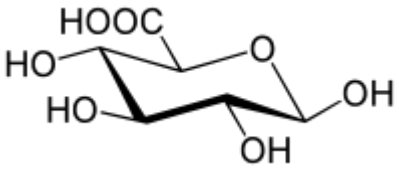
Hydrolysis

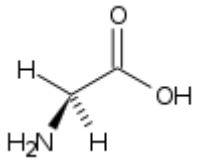
19. Ester

20. Amide

21. Epoxide

Nelle reazioni di Fase II si introducono nella molecola gruppi polari di dimensioni relativamente grandi .





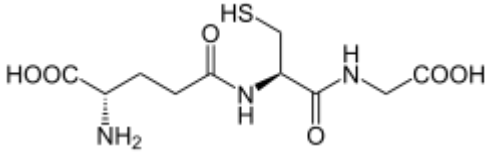


Table 3.15. Phase-II conjugation reactions [65]

Reaction	Functional group
Glucoronic acid	-OH, -COOH, -NH_2, -NH, -SH, -CH
Sulphate	aromatic -OH, aromatic -NH_2, alcohols
Glycine	-COOH
Acetyl	aromatic -NH_2, aliphatic -NH_2, hydrazides, -SO_2, -NH_2
Methyl	aromatic -OH, -NH_2, -NH, -SH
Glutathion	epoxides, organic halides

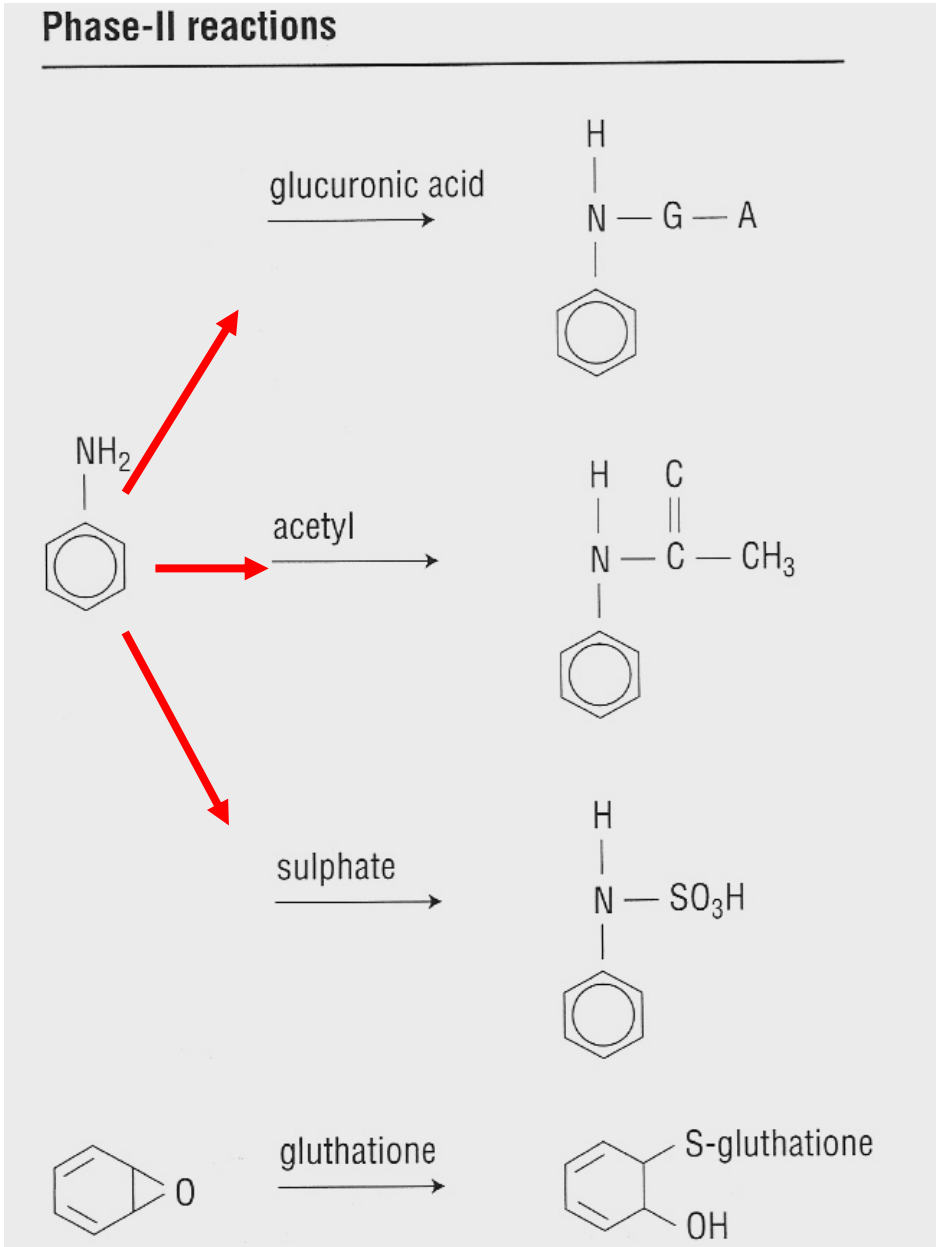


Figure 3.41. Some general phase-II biotransformation reactions involving aniline and benzene.

The general reaction for glucuronic acid conjugation is:

$$\text{UDPGA} + \text{R-XH} \xrightarrow{\text{GT}} \text{R-X-GA} + \text{UDP}$$

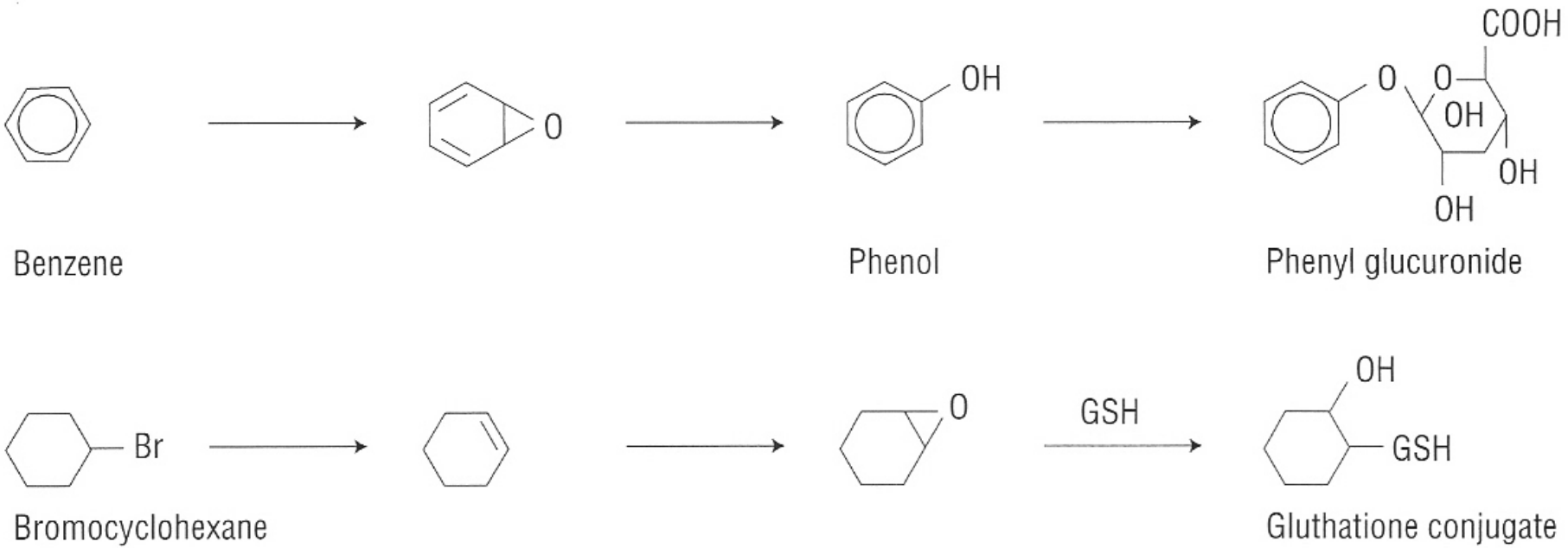
where X is O, COO or NH, UDPGA is uridine diphosphoglucuronic acid and GT is glucuronyltransferase.

The general reaction for sulphate conjugation is:

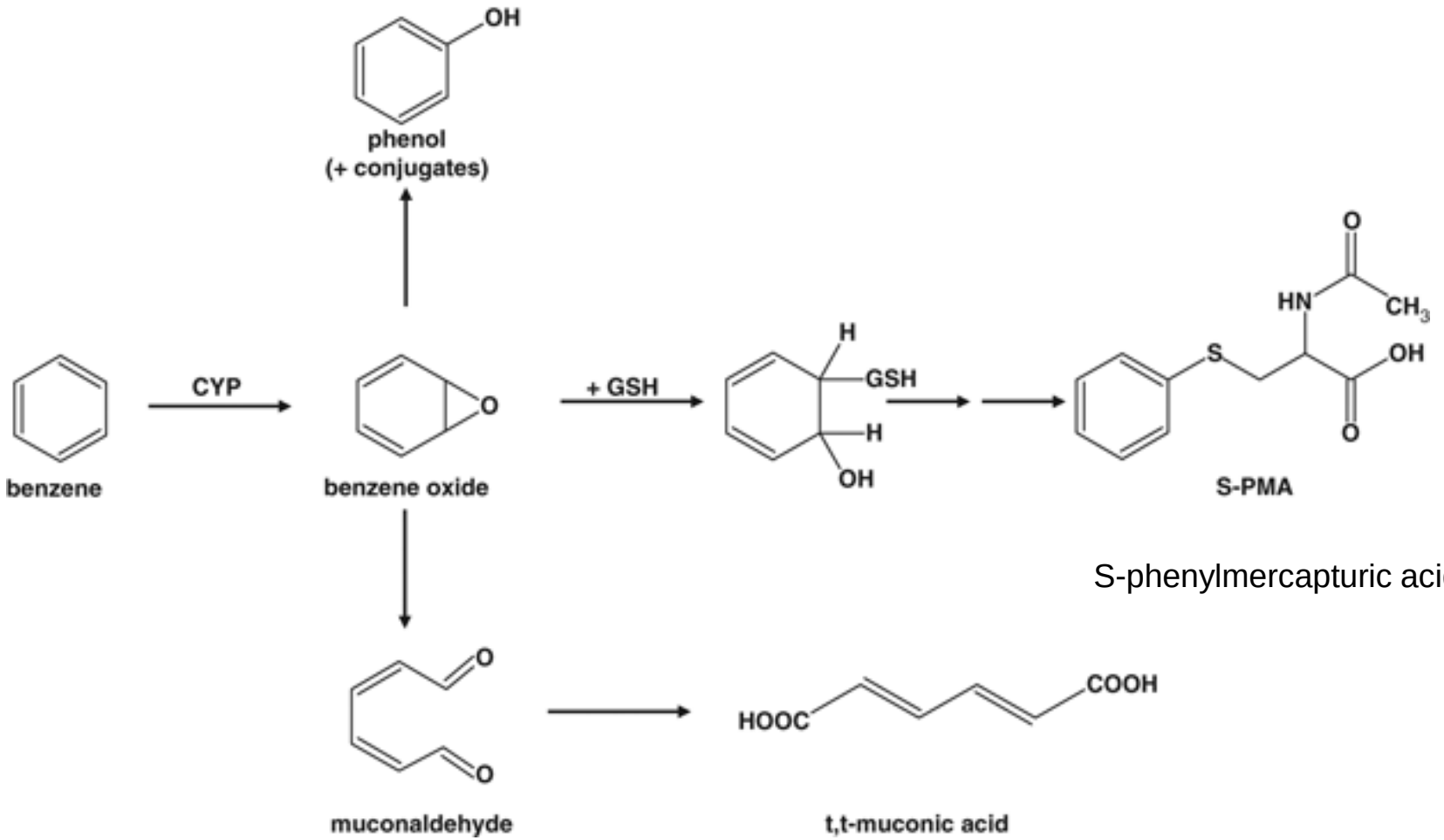
$$\text{PAPS} + \text{R-XH} \xrightarrow{\text{ST}} \text{R-X-SO}_3 + \text{PAP}$$

where X is O or NH, PAPS is 3'-phosphoadenosyl-5'-phosphosulphate, ST is sulfotransferase and PAP is 3',5'-adenosine diphosphate.

Phase-I + phase-II reactions

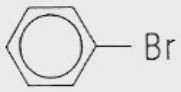
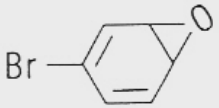
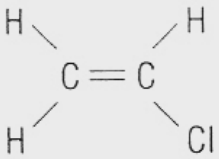
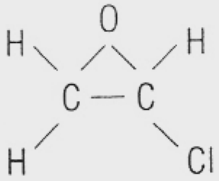
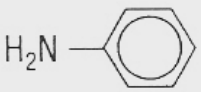
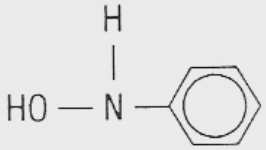
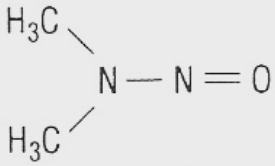


3.42. The role of phase-I and phase-II reactions in the mechanism of biotransformation of benzene and bromocyclohexane



S-phenylmercapturic acid (**SPMA**)

Prodotti tossici delle bio-trasformazioni

Compound	Proposed intermediate	Toxic effect
 Bromobenzene		Liver necrosis
 Vinyl chloride		Liver tumour
 Aniline		Methemoglobine
 Dimethylnitrosamine	CH_3^+	Carcinogenicity
Tetrachloromethane	CCl_3	Liver necrosis
Chloroform	$CHCl_3$,CCl_3	Kidney necrosis

3.43. The biotransformation of different xenobiotic compounds to reactive intermediates.

Table 3.16. Species variation for phenol conjugation with glucuronic acid and sulphate [64]

Species	Conjugation of phenol (percentage of total excretion)	
	glucuronic acid	sulphate
Pig	100	0
Rabbit	46	45
Rat	25	68
Man	23	71
Cat	0	87

$$E + S \underset{k_2}{\overset{k_1}{\rightleftarrows}} ES \underset{k_4}{\overset{k_3}{\rightleftarrows}} E + P$$

where E is enzyme, S is substrate, P is product, k_1, k_2, k_3 and k_4 are rate constants.

$$V = V_{max} [S] / (K_m + [S]) \qquad (3.67)$$

Eqz. di Michaelis Menten

Costante di Michaelis K_m,
valore caratteristico per reazione enzimatica, indipendente da concentrazione dell'enzima

http://users.unimi.it/biolstru/teaching/Cinetica_enzimatica.pdf

Biotrasformazione degli IPA

http://monographs.iarc.fr/ENG/
Monographs/vol92/mono92.pdf

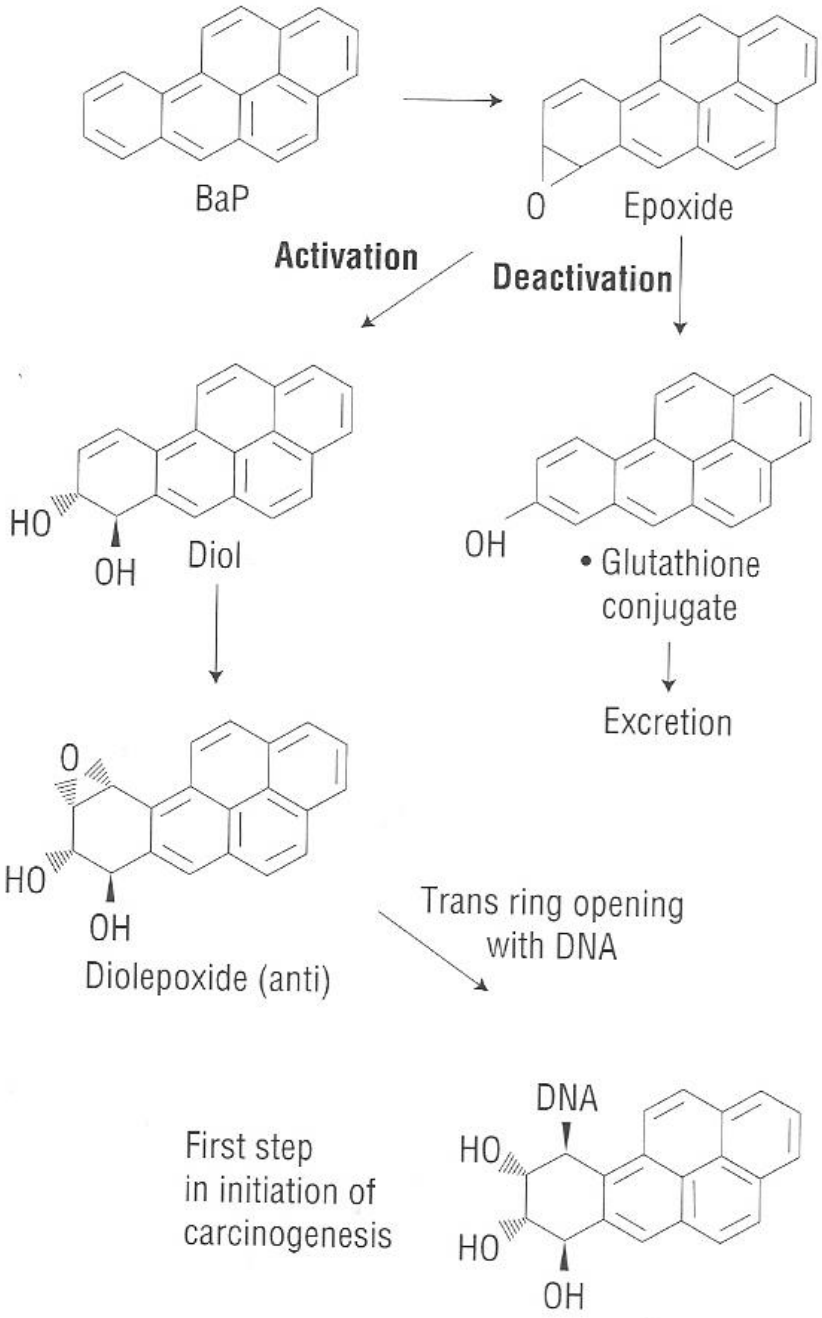
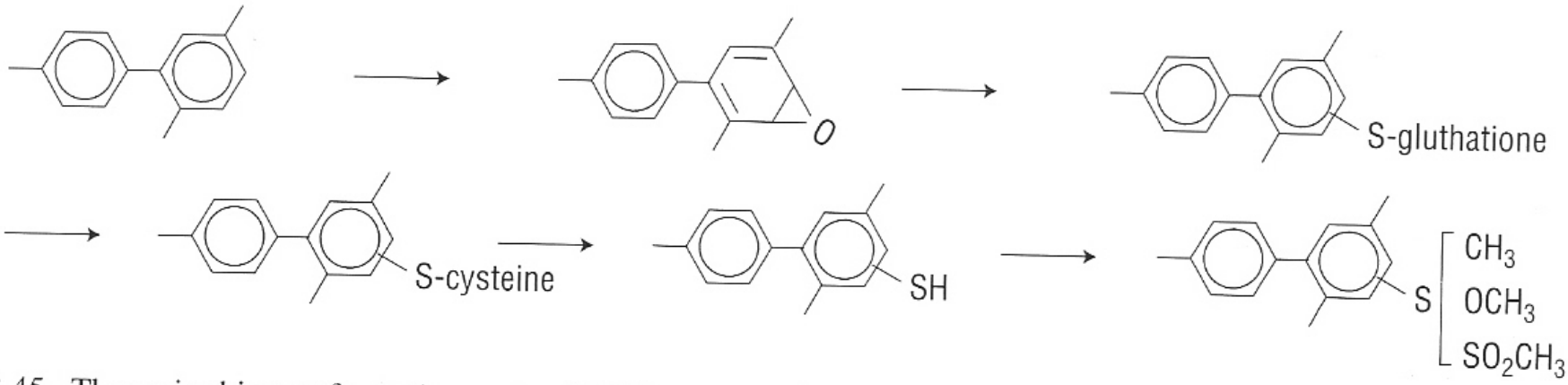


Figure 3.44. The biotransformation pathways of benzo(a)pyrene and binding to the DNA of reactive intermediates. From [66].



3.45. The major biotransformation route of PCBs. From Safe [72]. With permission.

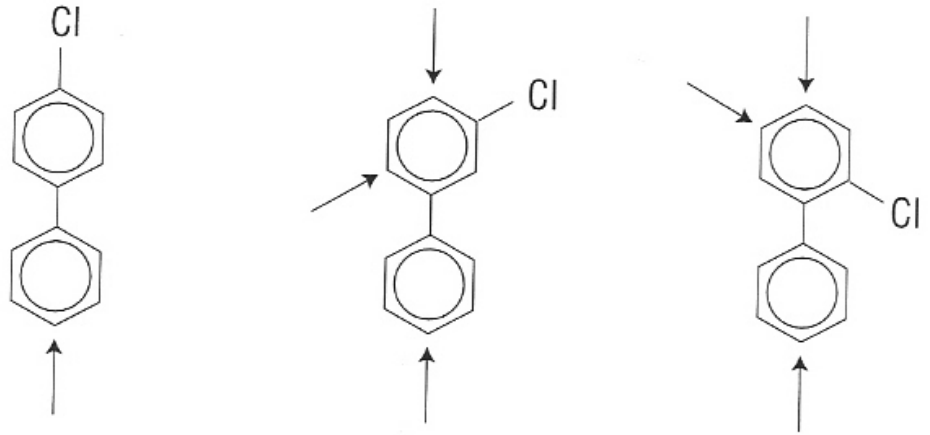
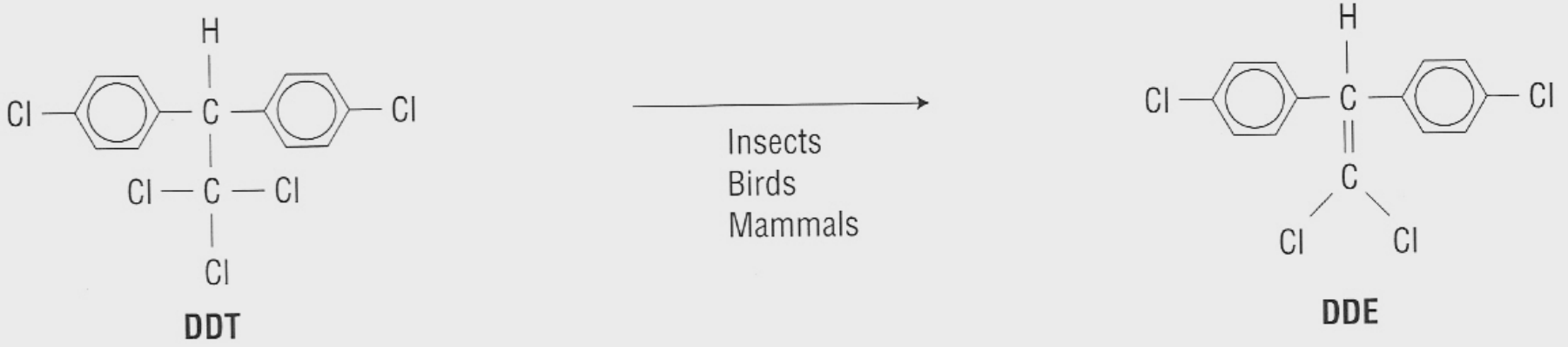
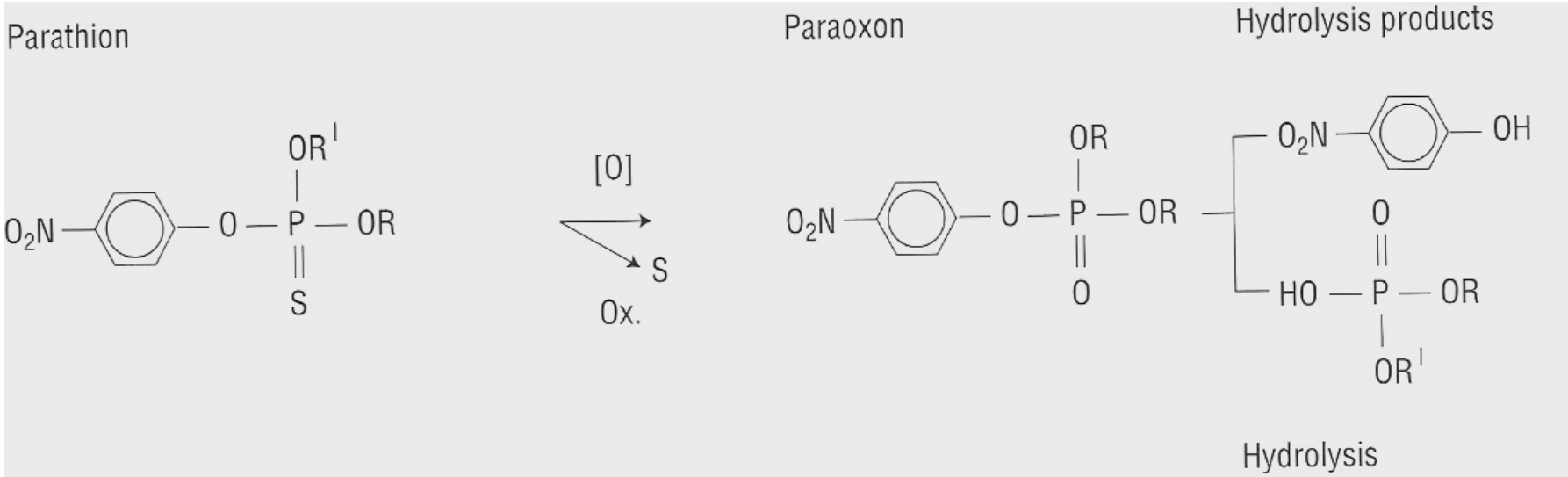


Figure 3.46. The preferred oxidation positions in a PCB molecule and the role of the chlorine position in the molecule in cytochrome P-450 catalyzed biotransformation reactions. From [67].



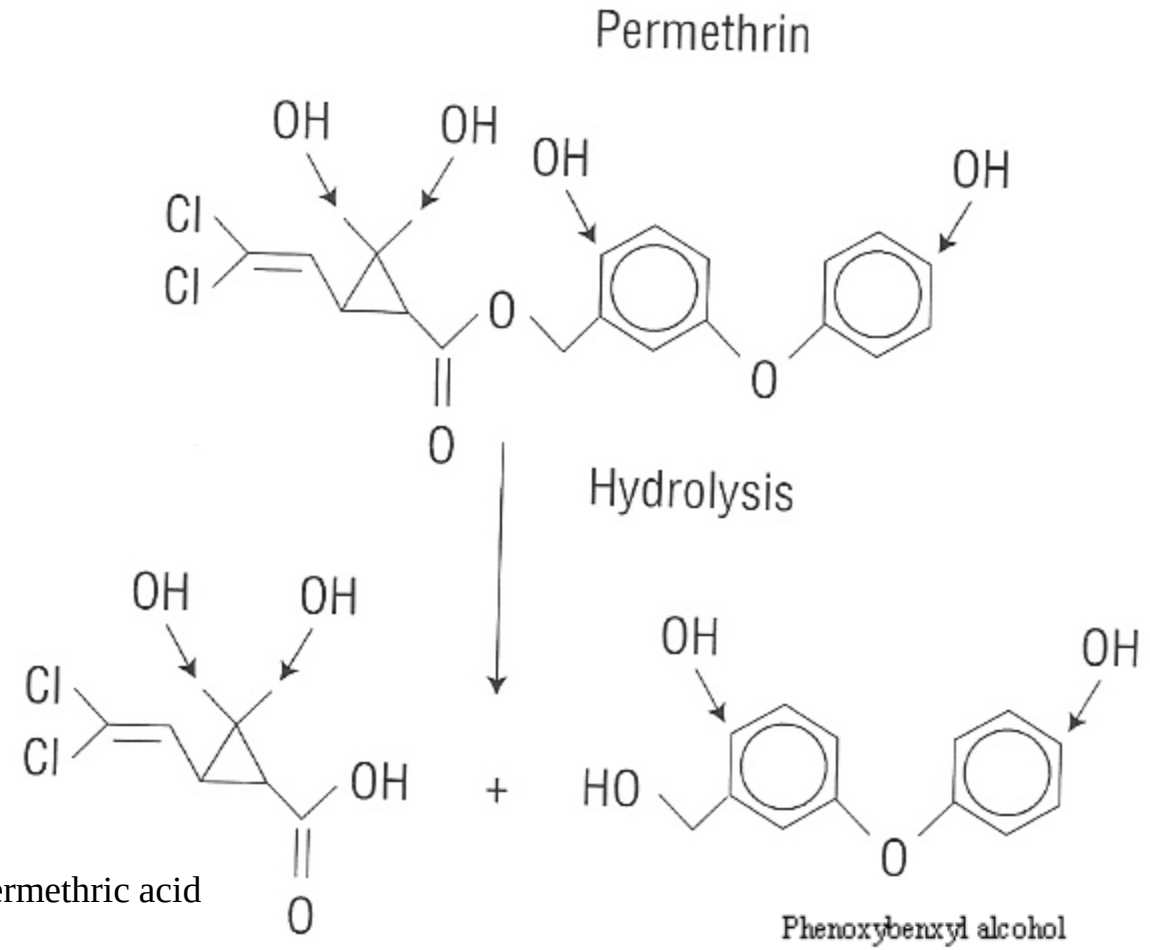
DDT **DDE**

3.47. The main route of biotransformation of DDT to DDE.



3.48. The biotransformation routes of organophosphorus compounds.

O,*O*-Diethyl *O*-(4-nitrophenyl) phosphorothioate



Dichlorovinyl acid; Permethric acid

Figure 3.49. The hydrolytic degradation of synthetic pyrethroids.

Table 3.17. Characteristics of the hepatic effects of PB and 3-MC [64]

Characteristic	PB	3-MC
Onset of effects	8-12 h	3-6 h
Time of maximal effect	3-5 d	1-2 d
Persistence of induction	5-7 d	5-12 d
Liver enlargement	marked	slight
Protein synthesis	large increase	small increase
Liver blood flow	increase	no effect
Biliary flow	increase	no effect
Enzymes:		
– cytochrome P-450 1A1 + 1A2	increase	no effect
– cytochrome P-450 2B1 + 2B2	no effect	increase
– NADPH-cytochrome reductase	increase	no effect

A proposito di composti organici fluorurati…

- http://www.oecd.org/ehs/pfc/Scheringer_OECD_webinar_2%20(2).pdf
- http://www.oecd.org/env/ehs/risk-management/PFC_FINAL-Web.pdf
- http://www.sciencedirect.com/science/article/pii/S0269749106006038
- http://gimle.fsm.it/30/4/01.pdf

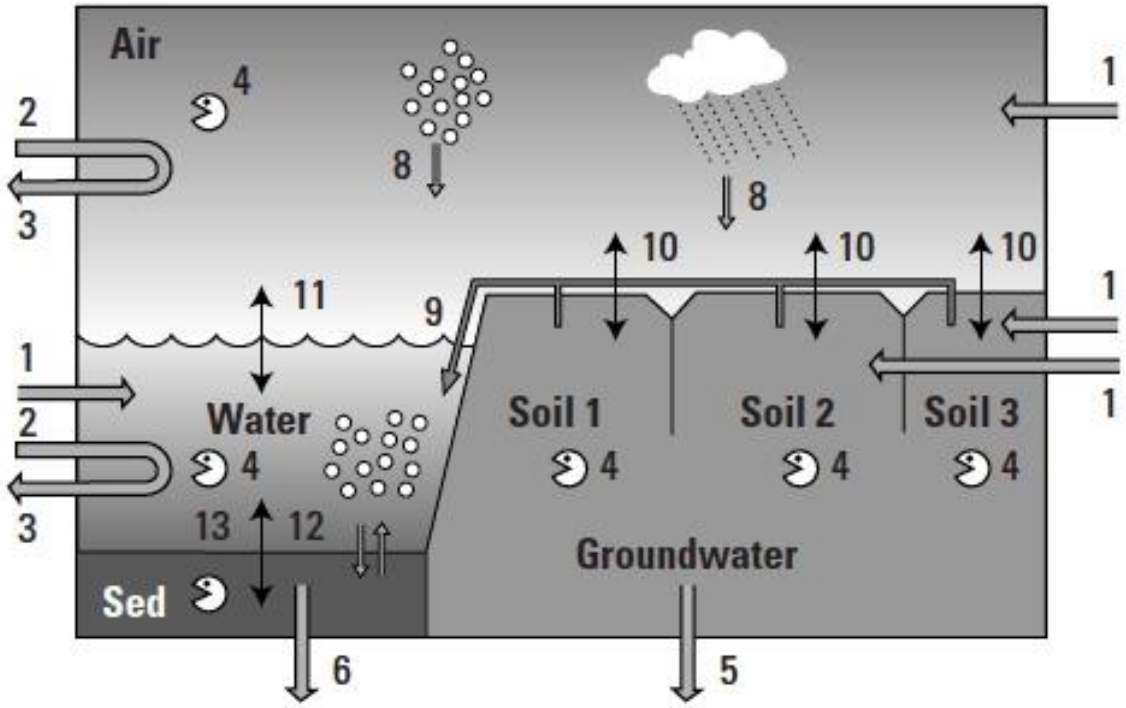


Figure 4.11. Diagram of a multimedia mass balance model concept. 1 = Emission, 2 = Import, 3 = Export, 4 = Degradation, 5 = Leaching, 6 = Burial, 7 = Wet deposition, 8 = Dry aerosol deposition, 9 = Run-off, 10, 11 = Gas absorption and volatilization, 12 = Sedimentation and resuspension, 13 = Sorption and desorption. From [61]

I processi di degradazione abiotica e biologica

Risk Assessment of Chemicals
Capitolo 4: environmental exposure assessment

Esposizione a *chemicals* degli organismi (umani inclusi) tramite l'ambiente

Valutazione dell'esposizione può avvenire tramite

- ***misure***
- altri metodi di stima - es. ***calcolo basato su modelli***

Esposizione per ***situazioni esistenti***: *misura* **o** *modelli*
Per rischi da ***nuove sostanze chimiche o situazioni***: solo modelli

Le *misure* possono sembrare aver meno incertezze dei modelli ma spesso eseguite su campioni raccolti in specifici luoghi e tempi, riflettendo specifiche variabilità spaziali e temporali. Spesso i piani di campionamento tendono a descrivere situazioni con concentrazioni elevate.

I *modelli* descrivono tendenzialmente situazioni medie o "tipiche" (utili nella valutazione dei rischi)

www.nature.com/jes/index.html

Journal of Exposure Science & Environmental Epidemiology

Welcome to *Journal of Exposure Science and Environmental Epidemiology*

Journal of Exposure Science and Environmental Epidemiology (JESEE) aims to be the premier and authoritative source of information on advances in exposure science for professionals in a wide range of environmental and public health disciplines. JESEE publishes original peer-reviewed research presenting significant advances in exposure science and exposure analysis, including development and application of the latest technologies for measuring exposures, and innovative computational approaches for translating novel data streams to characterize and predict exposures. Check out the full Aims & Scope here!

Announcement: Springer Nature and the International Society of Exposure Science are pleased to announce the new Editor-in-Chief of *Journal of Exposure Science and Environmental Epidemiology* (JESEE) – Dr. Elaine Cohen Hubal (Raleigh, NC USA). Dr. Cohen Hubal officially assumed the editorship in January 2017.

10 April 2017

- I modelli sono usati anche per valutare ***concentrazioni <u>biodisponibili</u>*** quando le misure risultano problematiche.

- *Idealmente* sia le conc di esposizione che le conc. per cui non c'è effetto avverso, dovrebbero essere espresse in termini di ***concentrazioni interne <u>al sito dell'organismo</u> in cui si estrinseca l'effetto tossico***, *ma* non abbiamo attualmente disponibili questi dati di concentrazioni interne di esposizione e di NEC interne -> *quindi* ci si deve basare su conc. nei comparti ambientali (introducendo incertezza, poiché il rapporto tra conc. interne ed esterne può essere diverso tra livelli di esposizione e NEC -> meglio impiegare conc. esterne biodisponibili).

Stadi per creare ed usare modelli:

- 1) **concettualizzazione** (decidere che tipo di rappresentazione della realtà si vuole creare)
- creatori di modelli e utilizzatori di modelli devon riflettere su *cosa* e *perché* viene modellato? Quali gli aspetti rilevanti per lo scopo e quali trascurabili?
- Modelli semplici in genere preferibili a m. sofisticati (servon più dati e lavoro, risultati usualmente più difficili da interpretare, comunicare e usare nel supporto alle decisioni).
- Criteri oggettivi di scelta

Box 4.1. Criteria for choosing the level of model sophistication

- Purpose of the model.
  For the purpose of identification of critical environmental compartments and *a priori* estimation of risks associated with the introduction of new chemicals, a relatively simple screening with a multimedia box model may be sufficient. Prediction of the effect of emission reduction on concentrations at specific times and places may require the use of a more sophisticated dynamic two or three-dimensional air, water or groundwater quality model.
- Acceptable uncertainty.
  The required level of confidence should follow from the use of the modelling results. If simple modelling demonstrates that the margin between the calculated concentration and the predicted no effect level (PNEC) is sufficiently great for the purpose of the modelling activity, no further increase in the level of confidence is required.

Vantaggio: concettualizzare le relazioni

- Possiamo usare la ns conoscenza dei processi per descrivere la *relazione* in termini di caratteristiche dell'ambiente e proprietà della specie chimica
- Utilità: valutare i *risultati di molti processi che avvengono simultaneamente* (i processi che influenzano le conc. delle specie chimiche sono relativamente ben compresi, ma la moltitudine di processi che agiscono in parallelo rende i risultati difficili da comprendere).

Box 4.2. Purpose of models

- Provide insight.
  Models provide a way to interpret observations logically. The use of models can help us to understand certain aspects of reality. They may help to identify cause-effect relationships that are not apparent in an initial review of the data. Used in this way, models primarily serve to provide insight into "how theory operates", as Lassiter put it, rather than "how the system operates" [1]. Models are useful for quantifying the implications of our assumptions about reality: they provide a way of testing the adequacy of the current state-of-the-art of theory to describe reality. A good way to gain better understanding with a model involves systematic variation of parameters to find the parameters which the model output is most sensitive to. This sensitivity-analysis procedure helps to identify the key processes and pathways for the chemical.
- Support decision-making.
  Modelling provides a means of eliminating the vagueness inherent to decision-making. Reasoning is made more explicit when the possible results of alternative strategies for risk reduction and the uncertainties associated with it are properly quantified. A powerful way to use models in decision-making is in the "what-if scenario", which can help to identify the most effective strategy.