

Non-First Order Degradation and Time-Dependent Sorption of Organic Chemicals in Soil

ACS SYMPOSIUM SERIES **1174**

Non-First Order Degradation and Time-Dependent Sorption of Organic Chemicals in Soil

Wenlin Chen, Editor

Syngenta Crop Protection, LLC, Greensboro, North Carolina

Aleksandar Sabljic, Editor

Institute Rudjer Boskovic, Zagreb, Croatia

Steven A. Cryer, Editor

Dow AgroSciences, LLC, Indianapolis, Indiana

Rai S. Kookana, Editor

CSIRO Land and Water, Glen Osmond, Australia

**Sponsored by the
ACS Division of Agricultural and Food Chemistry, Inc.**



American Chemical Society, Washington, DC

Distributed in print by Oxford University Press



Library of Congress Cataloging-in-Publication Data

Non-first order degradation and time-dependent sorption of organic chemicals in soil / Wenlin Chen, editor, Syngenta Crop Protection, LLC, Greensboro, North Carolina, Aleksandar Sabljic, editor, Institute Rudjer Boskovic, Zagreb, Croatia, Steven A. Cryer, editor, Dow AgroSciences, LLC, Indianapolis, Indiana, Rai S. Kookana, editor, CSIRO, Land and Water Flagship, Glen Osmond, Australia ; sponsored by the ACS Division of Agricultural and Food Chemistry, Inc.

pages cm. -- (ACS symposium series ; 1174)

Includes bibliographical references.

ISBN 978-0-8412-2978-5

1. Soil absorption and adsorption. 2. Soils--Organic compound content. 3. Agricultural chemicals--Biodegradation. 4. Organic compounds--Biodegradation. 5. Soil chemistry. I. Chen, Wenlin, 1962- editor. II. Sabljic, Aleksandar, editor. III. Cryer, Steven A., editor. IV. Kookana, Rai S., editor. V. American Chemical Society. Division of Agricultural and Food Chemistry. VI. Title: Sorption of organic chemicals in soil.

S592.5.N66 2014

631.4'32--dc23

2014038715

The paper used in this publication meets the minimum requirements of American National Standard for Information Sciences—Permanence of Paper for Printed Library Materials, ANSI Z39.48n1984.

Copyright © 2014 American Chemical Society

Distributed in print by Oxford University Press

All Rights Reserved. Reprographic copying beyond that permitted by Sections 107 or 108 of the U.S. Copyright Act is allowed for internal use only, provided that a per-chapter fee of \$40.25 plus \$0.75 per page is paid to the Copyright Clearance Center, Inc., 222 Rosewood Drive, Danvers, MA 01923, USA. Republication or reproduction for sale of pages in this book is permitted only under license from ACS. Direct these and other permission requests to ACS Copyright Office, Publications Division, 1155 16th Street, N.W., Washington, DC 20036.

The citation of trade names and/or names of manufacturers in this publication is not to be construed as an endorsement or as approval by ACS of the commercial products or services referenced herein; nor should the mere reference herein to any drawing, specification, chemical process, or other data be regarded as a license or as a conveyance of any right or permission to the holder, reader, or any other person or corporation, to manufacture, reproduce, use, or sell any patented invention or copyrighted work that may in any way be related thereto. Registered names, trademarks, etc., used in this publication, even without specific indication thereof, are not to be considered unprotected by law.

PRINTED IN THE UNITED STATES OF AMERICA

Foreword

The ACS Symposium Series was first published in 1974 to provide a mechanism for publishing symposia quickly in book form. The purpose of the series is to publish timely, comprehensive books developed from the ACS sponsored symposia based on current scientific research. Occasionally, books are developed from symposia sponsored by other organizations when the topic is of keen interest to the chemistry audience.

Before agreeing to publish a book, the proposed table of contents is reviewed for appropriate and comprehensive coverage and for interest to the audience. Some papers may be excluded to better focus the book; others may be added to provide comprehensiveness. When appropriate, overview or introductory chapters are added. Drafts of chapters are peer-reviewed prior to final acceptance or rejection, and manuscripts are prepared in camera-ready format.

As a rule, only original research papers and original review papers are included in the volumes. Verbatim reproductions of previous published papers are not accepted.

ACS Books Department

Editors' Biographies

Wenlin Chen

Wenlin Chen is a senior scientist at Syngenta Crop Protection, LLC, Greensboro, North Carolina, U.S.A. His area of work focuses on mathematical descriptions of pesticide environmental fate and transport and applications to water quality and ecological risk assessments. He holds a Ph.D. in soil science from Cornell University and has authored/co-authored more than 60 peer-reviewed papers, book chapters, and invited lectures/presentations. He has contributed to the development of pesticide exposure models, scenarios, and risk assessment methods in the U.S. and internationally through several scientific work groups including the FIFRA Environmental Model Validation Task Force, FQPA Drinking Water Exposure Work Group, Environmental Exposure Work Group, and IUPAC Advisory Committee on Crop Protection Chemistry. His current interests include kinetics of rate-limited metabolism, sampling design, and statistical modeling of environmental monitoring data.

Aleksandar Sabljic

Aleksandar Sabljic is Head of Department of Physical Chemistry at Institute Rudjer Boskovic in Zagreb, Croatia since 2002. His research interests and expertise span a wide range of subjects but his recent research is focused on modeling sorption of organic chemicals in soil, their biodegradation in aquatic and soil environments and tropospheric degradation of volatile/semi-volatile chemicals.

After receiving Ph.D. in chemistry from the University of Zagreb (Croatia), he was the Fogarty International Fellow at National Institutes of Health, Bethesda, Maryland (1981-1985). For an extended period (1988-1998), he was Visiting Scientist at Forschungszentrum Karlsruhe and University of Karlsruhe in Germany.

Steven A. Cryer

Cryer received a B.S. in chemical engineering from Texas A&M University, and master's and doctorate degrees in chemical engineering from Cornell University, with emphasis in applied math and hydrodynamic stability. Steve is a strong industrial leader advocating new approaches and scientific advancement to address issues relevant for the agrochemical community, authoring or coauthoring over 80 peer-reviewed papers and conference abstracts, 6 book chapters, multiple

invited presentations and guest lectures, and expert panel participation in areas of wet granulation, pesticide runoff, and volatility of organic chemicals from soil. Steve has been on the adjunct faculty at several Indiana University Departments and has 25 years of experience with Dow AgroSciences.

Rai S. Kookana

Dr. Rai Kookana is a Chief Research Scientist with CSIRO and is also affiliated as a Professor in the School of Agriculture, Food and Wine (University of Adelaide). With a Ph.D. from the University of Western Australia (1989), he has been involved in pesticide research for last 25 years. Dr. Kookana's current research interests include fate of nanoparticles, pesticides and micropollutants (e.g. pharmaceuticals and personal care products) in the environment. He has published 175 journal papers, 15 book chapters, with an H-Index (ISI) of 33 and a total citation > 4500. Dr Kookana has edited three books on environmental contaminants. He is on the editorial boards of 4 international journals. In 2012, Dr. Kookana was elected Fellow of the Soil Science Society of America.

Chapter 1

Introduction

**Wenlin Chen,^{*}1 Aleksandar Sabljic,² Steven A. Cryer,³
and Rai S. Kookana⁴**

¹Syngenta Crop Protection, LLC, P.O. Box 27419-8300,
Greensboro, North Carolina 27419-8300, U.S.A.

²Department of Physical Chemistry, Institute Rudjer Boskovic,
POB 180, HR-10002 Zagreb, Croatia

³Dow AgroSciences, LLC, 9330 Zionsville Road,
Indianapolis, Indiana 46268, U.S.A.

⁴CSIRO, Land and Water Flagship, PMB 2, Glen Osmond 5064, Australia

^{*}E-mail: Wenlin.chen@syngenta.com.

Pesticides are essential tools for crop protection and disease prevention. These agricultural chemicals (and their associated uses) continue to be subject to increased regulatory scrutiny, even though modern pesticides have become safer, more effective, and target specific. Pesticide persistence, off-target movement to ground and surface water systems, and potential for impacting non-target organisms are the major focus for regulatory assessments. Sorption and degradation are among the dominant processes that determine the fate and ecological risk of pesticides in the environment. This book addresses pesticide sorption and degradation processes in the context of regulatory evaluation, yet with a special focus on the chemistry-soil-environment interactions to better quantify the increasingly observed non-first-order and time-dependent behavior in the environmental fate studies.

Degradation of agricultural chemicals is commonly described by pseudo first-order (PFO) kinetics, with the underlying assumption that the rate of degradation is only proportional to the concentration of the degrading compound. The other “reactant” (or reactants) involved in the degradation process is

assumed to be invariant or can be effectively incorporated into the PFO rate constant. For enzyme-catalyzed degradation or biodegradation, the process may become rate-limited when the substrate (i.e. the chemical of interest) is not freely available to microbial metabolism (I), resulting in poor fit of the PFO kinetics to experimental observations. This is particularly true when sorption and diffusion are prominent in controlling mass transfer between the cell surfaces and microbial-absent regions in soil where chemicals are adsorbed, bound or physically entrapped (e.g., in inter-/intra-particle micropores). In such cases, non-first-order degradation and time-dependent sorption may occur simultaneously. Non-first-order degradation may also be induced by microbial dynamics when bioactivity fluctuates over the course of a laboratory study or due to temperature/moisture and/or other agronomic and environmental changes under field conditions.

A common practice to describe pesticide sorption (physical and/or chemical process by which the pesticide becomes bound to a solid substrate) is to assume equilibrium (steady state) during partitioning between the solution and solid phases. In contrast, time-dependent sorption typically describes the process of increasing sorption (or decreasing in a desorption mode) of an organic compound with time in soil. Various physical/chemical mechanisms responsible for time-dependent sorption may include inter-/intra-particle micropore diffusion, surface site adsorption, partitioning, and hydrogen or chemical bonding (2–4).

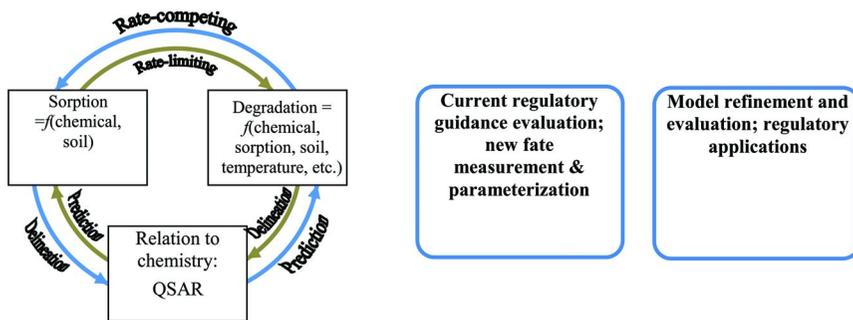
When non-first-order degradation and time-dependent sorption exist, the conventional PFO and equilibrium sorption approaches may not be adequate predictors of the fate and transport behavior of agriculturally important chemicals. The recent publications (5, 6) of regulatory guidance for calculating non-first-order kinetics for pesticide environmental risk and exposure assessments, both in the European Union (EU) and North America Free Trade Agreement (NAFTA), have renewed the interest in refining the measurements, interpretation and use of kinetic data. This ACS book summarizes the combined work recently presented at the 246th ACS National Meeting symposium of Non-First-Order Dissipation and Time-Dependent Sorption of Organic Chemicals in Soil: Measurement, Modeling, and Impact on Environmental Exposure Predictions, September 8 - 12, 2013, Indianapolis, Indiana, USA; and the findings from the International Union of Pure and Applied Chemistry (IUPAC) research project (2010-018-2-600): Review of Pesticide Environmental Fate Parameters and Their Quantitative Relationship with Soil and Climate Conditions (7). Conventional and novel approaches for time-dependent sorption and degradation presented in this book will benefit a large audience of readers, including the regulatory community, academia, government, and industry scientists.

The chapters are arranged according to the three general topics as illustrated in the diagram below. The book starts (Chapter 2) with the interactions of the fate processes (sorption and degradation) and their relationship with chemistry (quantitative structure-activity relationship, or QSAR) and the soil and environmental conditions (Chapters 3, 4, and 5). Evaluation of current NAFTA regulatory kinetics guidance and an overview of using time-dependent sorption studies in EU regulatory exposure assessment are provided in Chapters 6 and 7, respectively. Approaches for data delineation of degradation kinetics and

parameterization are presented in Chapters 8, 9, and 10. New experimental design and methods to measure and quantify time-dependent sorption and irreversibility are described in Chapters 11, 12, 13, and 14. The last section of the book is dedicated to the development of the coupled sorption and degradation kinetics on the EU FOCUS-PRZM model (Chapter 15) and followed by several model evaluation and validation case studies to demonstrate the impact of non-first-order degradation and time- and soil-dependent sorption on the overall environmental fate and transport processes in field conditions (Chapters 16, 17, and 18).

Interaction of fate processes, chemistry and the environment

Regulatory application, measurement, parameterization, and modeling



It is anticipated the state of knowledge and information presented in this book will provide the foundation for stimulating discussion and development of new approaches, leading to more accurate pesticide environmental fate and exposure predictions through improved study measurements, model parameterization, and use of sound kinetics of degradation and sorption algorithms. We realize that the conventional use of the PFO kinetics and instantaneous sorption assumptions has its advantages and may be valid in many cases. However, the text presented here, including discussion of new experimental methods, analysis of kinetics, structure-activity relationships, and refined modeling tools will provide valuable insights to the reader on this topic. We hope that this book will be useful to the broad agrochemical research community including environmental scientists, risk assessors/regulators, students, and general practitioners in environmental exposure, risk assessment, and risk management.

Acknowledgments

The editors extend their sincere thanks to all contributing authors for their hard work to make this book possible, and to all the peer-reviewers who dedicated time to the quality of the book publication. Special thanks are due to Scott Yates and Dirk Young for coordinating the ACS symposium. We acknowledge the financial support from the American Chemical Society Agro-Chemical Division, IUPAC, and Syngenta Crop Protection, LLC, for sponsorship of the symposium and the IUPAC research project (2010-018-2-600). Guidance/assistance received

from the ACS Editorial staff, namely, Julia Johnson, Tim Marney, Arlene Furman, Bob Hauserman, and Ashlie Carlson are greatly appreciated. A special thanks to Julia Johnson for her day-to-day assistance, patience, and always timely response during the book preparation. Cover art photograph is “Barley harvest in Washington’s Palouse Hills”, image number K3937-14, downloaded from <http://www.ars.usda.gov/News/docs.htm?docid=23559>.

References

1. Bosma, T. N. P.; Middeldorp, P. J. M.; Schraa, G.; Zehnder, A. J. B. *Environ. Sci. Technol.* **1997**, *31*, 248–252.
2. Brusseau, M. L.; Rao, P. S. C.; Gillham, R. W. *Crit. Rev. Environ. Control* **1989**, *19*, 33–99.
3. Chen, W.; Wagenet, R. *J. Environ. Sci. Technol.* **1995**, *29*, 2725–2734.
4. Pignatello, J. J. *Adv. Agron.* **2000**, *69*, 1–73.
5. NAFTA Technical Working Group on Pesticides. *NAFTA Guidance for Evaluating and Calculating Degradation Kinetics in Environmental Media*; 2012; http://www.epa.gov/oppefed1/ecorisk_ders/degradation_kinetics/NAFTA_Degradation_Kinetics.htm.
6. FOCUS Work Group on Degradation Kinetics. *Guidance Document on Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration*, Report of the FOCUS Work Group on Degradation Kinetics, EC Document Reference Sanco/10058/2005 version 2.0; 2006; <http://focus.jrc.ec.europa.eu/dk/docs/finalreportFOCDegKin04June06linked.pdf>.
7. Chen, W. *Chem. Int.* **2011**, *33*, 23.

Chapter 2

Coupled Sorption and Degradation Kinetics and Non-First Order Behavior

Wenlin Chen,^{*1} Volker Laabs,² Rai S. Kookana,³
and William C. Koskinen⁴

¹Syngenta Crop Protection, LLC, P.O. Box 18300,
Greensboro, North Carolina 27419-8300, U.S.A.

²BASF SE, Crop Protection, Speyerer Straße 2,
D-67117 Limburgerhof, Germany

³CSIRO Land and Water, PMB 2, Glen Osmond,
Adelaide, South Australia 5064, Australia

⁴University of Minnesota, Soil, Water, and Climate, 6028A,
1991 Upper Buford Circle, St. Paul, Minnesota, 55108, U.S.A.

*E-mail: wenlin.chen@syngenta.com.

The spatial distribution of organic compounds in the microscopic soil/pore-water system due to sorption has fundamental implications on determining first-order or non-first order behaviour and assessing bioavailability/biodegradability. If only the fraction of the organic compounds in the microbe-accessible region (e.g., soil pore water) is directly subject to intracellular transformation, sorption into microbe-absent regions (e.g., intra-particle/intra-aggregate micro-pores/interstitial spaces) may become rate-limiting to biodegradation, thus a non-first order decline may be expected in the soil-water system. In this paper, several data sets with direct measurements of soil pore water concentrations are used to elucidate the effect of sorption/desorption on biodegradation. Macro rate constants equivalent to the Double First-Order in Parallel (DFOP) model are derived for gauging the non-first order behavior and for calculating the micro kinetic rate constants of sorption and biodegradability from standard laboratory soil metabolism and batch sorption studies. Two new bioavailability factors (short-term and long-term) are developed to delineate the confounding effect of sorption

and a compound's specific biodegradability on the overall degradation rate in the bulk soil system. The bioavailability factors are shown to be useful in the development of predictive regressions for degradation using soil and environmental factors. Discussions on data interpretation and implications for coordinated study designs of different fate studies are provided.

Introduction

Many published and regulatory required soil metabolism studies have shown that microbial degradation of pesticides can be a non-first order process. Various non-first order degradation models have been proposed to best fit data and to derive representative or worst-case half-life values in order to satisfy the input requirement of the regulatory models for environmental exposure and risk assessments (1, 2). None of these models, however, are mechanistically based, i.e., they are difficult to use for interpreting the observed data and lack of insight into the underlying processes which require cross-examination of other environmental fate studies such as sorption. The aim of this chapter is to offer an approach that couples the two most important fate processes, sorption and degradation, and delineates the effects of soil and other environmental conditions on non-first order behavior.

Interaction between sorption and degradation of organic chemicals in soil is not a new phenomenon. The root cause of the interdependent relationship is the microscopic heterogeneity in distributions of chemical substrates and microbial degraders in the soil pore that prevents metabolism from occurring at the right place and right time. On a microscopic soil pore scale, sorption separates substrate (pesticide) from its degrader (microorganisms) by mass transfer (primarily via diffusion) of the substrate molecules to the soil intra-aggregate/intra-particle pores/interstitial space or organic matrix where microbial access is limited. Soil micro pores with diameters $<0.1 \mu\text{m}$ are abundant while typical size of indigenous bacteria is larger than $0.5 \mu\text{m}$ in diameter³. Bacteria (single or in colonies) typically inhabit in soil pores $\geq 2 \mu\text{m}$ in diameter and the majority of soil pores are smaller than this size with soil moisture content at field capacity levels (3, 4). As a result, physical exclusion of microbes from the micro pores/interstice of soil particles/micro-aggregates may imply that only the fraction of organic compounds in the microbe-accessible region (e.g., in the bulk soil solution or aqueous phase) may be directly subject to intracellular transformation (3–6). This may also include substances sorbed (reversible or irreversible) into the organic matrix in the microbe-accessible regions such as larger pores or micro surfaces in desolate areas. Mass transfer of organic compounds from the microbe-absent regions (or sorbed phase as a general term) thus may become a rate-limiting step to microbial degradation in the soil pore system.

Conceptually, sorption and degradation are initially two competing processes for available molecules in soil pore water when a compound is freshly applied (Figure 1). As more molecules become adsorbed and transferred via diffusion in to the micro pores or intra-particle structure inaccessible to microbes, degradation

rate in the aqueous phase may become limited/controlled by the release speed from the microbial absent zones depending on the intrinsic biodegradability of the compound.

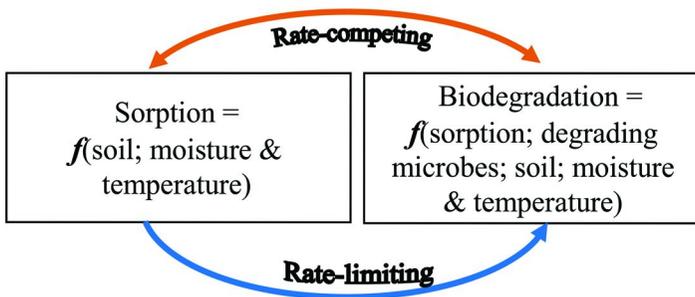


Figure 1. Sorption and biodegradation as a function of environmental factors and their mutual relationship in the soil-pore water system.

Soil variables influencing both pesticide sorption and degradation processes may operate in two ways: (i) variables that predominantly influence the sorption of substances and thereby change the availability of substances for degradation (7); and (ii) variables that indeed influence sorption and degradation processes independently from each other. Sometimes these two mechanisms may not be differentiated easily, as soil parameters are often interrelated and may thereby influence degradation predominantly via their correlation with soil sorption. The independent and/or interrelated soil and environmental variables can influence the interactions between degradation and sorption differently under different macroscopic conditions. Therefore, delineating the exact impacts by various variables requires a detailed description of the two interacting processes in the micro soil-water environment.

In this chapter, we first present a set of mathematical solutions for the coupled sorption and degradation kinetics. Several published literature data sets with direct measurements of soil pore water concentrations are used to elucidate the effect of sorption on degradation. Two macro rate constants equivalent to the Double First-Order in Parallel (DFOP, FOCUS Guidance) are defined and used to measure system deviation from first-order and to estimate micro rate parameters from standard laboratory soil metabolism and batch sorption studies. Two new bioavailability factors are proposed to help delineate the coupled influence of sorption and biodegradability on the overall degradation of the bulk soil system. Attempt is also made to investigate predictive relationships of degradation rates with the new bioavailability factors and soil/environmental variables available from published literature data.

For the sake of simplicity, we use degradation interchangeably with biodegradation on the understanding that degradation through abiotic processes such as hydrolysis is not considered in the context of the discussion herein and that the final breakdown product is not necessarily CO_2 .

Theory

The interactions between sorption and degradation on the pore scale can be conceptualized as a two-step process (Figure 2): 1) mass transfer between the sorbed phase and microbial cell surface in the bulk solution; and 2) biological uptake and transformation (8). For chemicals in the sorbed phase, mass transfer primarily involves desorption (i.e., from the sorbing surfaces inside the nano/micro pores or interstice) and diffusion to the bulk soil solution where microbial colonies reside. For chemicals in the bulk soil solution, the mass transfer process plays a competing role for the dissolved molecules by diffusion into the microbial-absent regions and/or adsorption onto the micro surfaces of soil particles.

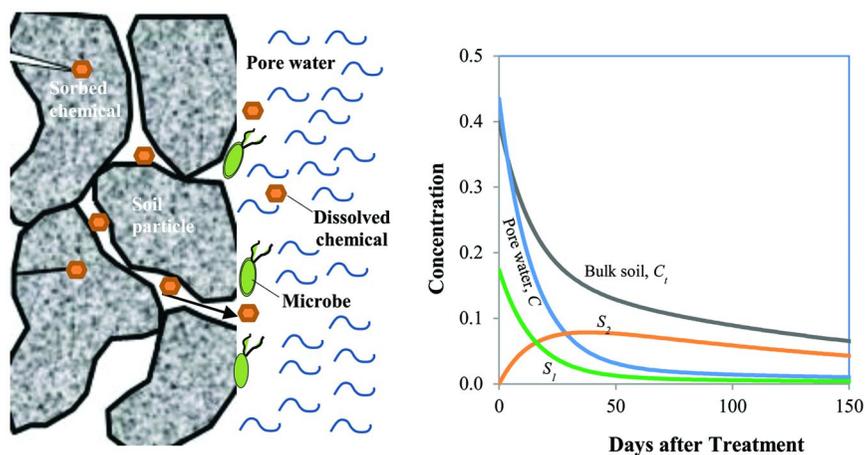


Figure 2. Schematic representation of the soil pore scale distributions of pesticide molecules and microorganisms in the soil-water system (left). The concentration-time course on the right was simulated by Eqs. 5-8 (with parameters: $f=0.2$, $\mu_w=0.1 \text{ d}^{-1}$, $\alpha=0.01 \text{ d}^{-1}$, $K_d=2 \text{ ml/g}$, and $\rho/\theta=3.25 \text{ g/cm}^3$). Concentrations in the aqueous phase (C) and on the instantaneous sorption sites (S_i) decrease faster than the total bulk soil concentration (C_i) which exhibits a clear non-first order decline due to the formation (adsorption) and decline (desorption) on the time-dependent sorbed phase (S_2). (see color insert)

A pseudo first order (PFO) reaction can be used to simplify the lumped microbial uptake and subsequent intra-cellular transformation process given that concentrations of organic chemicals are generally low in the bulk soil solution (8). Since degradation on the sorbed phase is expected to be minimal, the mass balance of an organic chemical in a bulk soil unit can be written:

$$\frac{d}{dt} [\theta C + \rho S] = -\mu_w \theta C \quad (1)$$

Where C is concentration in the dissolved phase; $\mu\text{g/L}$; S is concentration in the adsorbed phase, $\mu\text{g/g}$; θ is volumetric soil moisture content, cm^3/cm^3 ; ρ is soil bulk density, g/cm^3 ; μ_w is degradation rate constant in the soil pore water or aqueous phase, day^{-1} ; t is time, day.

The sorption term (S) in Eq. 1 is described by a two-site kinetics model, which takes into account the bi-phasic behaviour commonly observed in the adsorption-time curve where the initial portion of adsorption takes place quickly and is then followed by a gradual time-dependent phase (9–14). The first type of sorption site(s) (denoted as S_1) is presumably related to the sorbing regions/micro surfaces directly exposed to the soil bulk solution so that sorption in these areas may reach local equilibrium almost instantaneously. The second type of sorption sites (S_2) may represent the sorbing regions inside the micro pores/interstice where diffusion through the micro tortuous space/channels is a slow time-dependent process (15). Assuming Freundlich equilibrium sorption for S_1 , the two-site sorption model can be expressed as the equations below:

$$S = S_1 + S_2 \quad (2)$$

$$S_1 = fK_f C^{1/n} \quad (3)$$

$$\frac{dS_2}{dt} = \alpha[(1-f)K_f C^{1/n} - S_2] \quad (4)$$

Where S_1 is the amount sorbed at the equilibrium sorption sites, $\mu\text{g/g}$; S_2 is the amount sorbed at the time-dependent sorption sites, $\mu\text{g/g}$; f is soil fraction of the equilibrium sorption sites, dimensionless; K_f is Freundlich sorption coefficient when ultimate sorption equilibrium is reached, unit dependent on S_1 and C ; n is Freundlich constant; α is desorption rate constant (or mass transfer coefficient), day^{-1} . Other variables are defined in Eq. 1. For linear sorption isotherms (i.e., $n=1$), the Freundlich coefficient K_f is traditionally termed as sorption partition coefficient and denoted by K_d (unit: ml/g). When K_d is normalized by soil organic carbon, the resulting parameter is denoted as K_{oc} (unit: ml/g).

For linear equilibrium sorption, Eqs. 1-4 can be solved analytically with initial conditions (i.e., at $t=0$, $C=C_0$; $S_1=fK_dC_0$; and $S_2=0$) (16–18). For consistency and complete expressions of defined parameters and variables, several closed-form solutions of key variables are provided below:

$$C = \frac{C_0}{(\lambda_1 - \lambda_2)} [(\alpha + \lambda_1) \exp(\lambda_1 t) - (\alpha + \lambda_2) \exp(\lambda_2 t)] \quad (5)$$

$$S_1 = fK_d C \quad (6)$$

$$S_2 = \frac{\alpha(1-f)K_d C_0}{(\lambda_1 - \lambda_2)} [\exp(\lambda_1 t) - \exp(\lambda_2 t)] \quad (7)$$

$$C_t = C_{t0} [A \exp(\lambda_1 t) + (1-A) \exp(\lambda_2 t)] \quad (8)$$