

THESIS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY

Contributions to Emission, Exposure and Risk Assessment of  
Nanomaterials

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Environmental Systems Analysis  
Energy and Environment  
CHALMERS UNIVERSITY OF TECHNOLOGY  
Gothenburg, Sweden 2012

Contributions to Emission, Exposure and Risk Assessment of Nanomaterials

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ISBN 978-91-7385-737-6

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Doktorsavhandlingar vid Chalmers tekniska högskola

Ny serie nr 3418

ISSN 0346-718X

ESA report 2012:11

ISSN: 1404-8167

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Cover: Collage based on the orange environmental hazard pictogram that has now been replaced by a new hazard pictogram according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS). The black dots symbolize nanoparticles and the structure in the upper right corner symbolizes the nanomaterial graphene.

Chalmers Reproservice

Gothenburg, Sweden 2012

## **ABSTRACT**

In recent years, synthetic nanomaterials have begun to be produced and used in increasingly larger volumes. These materials may cause new or increased risks to the environment, but no harmonized methods for structured assessment of their environmental risks exist. The main aim of this thesis is to contribute to the development of emission and exposure assessment methods, and thus also risk assessment methods, for nanomaterials. The second aim is to apply developed methods to specific nanomaterials. The nanomaterials assessed were titanium dioxide nanoparticles, silver nanoparticles, and graphene.

Starting from the two methods of risk assessment of chemicals and substance flow analysis, three different methods were outlined. The first method is called particle flow analysis, and can be used to assess current and future potential particle number-based emissions of nanoparticles. The second method is an exposure model for nanoparticles based on colloidal stability. This method can be used to derive particle number-based predicted environmental concentrations of nanoparticles. The third method is exposure modeling of nanomaterials based on partitioning factors, a method that can be used to derive mass-based predicted environmental concentrations.

By applying the particle flow analysis method, it was shown that antibacterial clothing is a large source of particle number-based emissions of silver nanoparticles, and could become an even larger source. Applying the same method to titanium dioxide nanoparticles showed that both the currently highest, and potentially also the future highest, particle number-based emissions come from sunscreen. By applying the exposure method based on partitioning factors, it was shown that if the silver content of antibacterial clothing is as high as some measurements have indicated, there is considerable risk of high silver levels in wastewater treatment sludge and in agricultural land if the sludge is applied as fertilizer. A review of risk-related properties of graphene showed that the risk-related data is very scarce, but what is available gives reason for concern in relation to high potential emissions, high persistence, hydrophobicity, and considerable toxicity. The developed methods, case study results, and some reflections and suggestions for future research together constitute contributions to emission assessment, exposure assessment, and risk assessment of nanomaterials.

Keywords: Nanomaterials, nanoparticles, emission assessment, exposure assessment, risk assessment, titanium dioxide, silver, graphene, particle flow analysis, substance flow analysis.



## Appended papers

This thesis is based on the work contained in the following papers:

### **Paper I**

Arvidsson, R., S. Molander, B. A. Sandén, and M. Hassellöv (2011). Challenges in exposure modeling of nanoparticles in aquatic environments. *Human and Ecological Risk Assessment*, 17(1): 245–262.

### **Paper II**

Arvidsson, R., S. Molander, and B. A. Sandén. (2011). Particle flow analysis: Exploring potential use phase emissions of TiO<sub>2</sub> nanoparticles from sunscreen, paint and cement. *Journal of Industrial Ecology*, 16(3): 343-351.

### **Paper III**

Arvidsson, R., S. Molander, and B. A. Sandén. (2011). Impacts of a silver-coated future: Particle flow analysis of silver nanoparticles. *Journal of Industrial Ecology*, 15(6): 844-854.

### **Paper IV**

Arvidsson, R., S. Molander, and B. A. Sandén. (2011). Assessing the environmental risks of silver nanoparticles from clothes to sludge and soil organisms. Accepted for publication in *Human and Ecological Risk Assessment*.

### **Paper V**

Arvidsson, R., S. Molander, and B. A. Sandén. (2011). Reviewing the potential environmental and health risks of the nanomaterial graphene. Accepted for publication in *Human and Ecological Risk Assessment*.

## Acknowledgments

I gratefully acknowledge the support and wisdom provided by my main supervisor Sverker Molander and my second supervisor Björn Sandén during this work. In addition to these two, I thank my examiner Anne-Marie Tillman who has provided important input from which this work has benefitted in many ways. I also thank my colleagues and fellow PhD candidates at the division of Environmental Systems Analysis, especially Kristin Fransson who has read and commented on much of this work. My thanks also go to my co-author Martin Hassellöv.

I gratefully acknowledge the funding that I have received from a number of funding agencies: the Swedish Research Council for Environment, Agricultural Sciences and Spatial Planning (Formas) through the research projects NanoRisk and NanoSphere; the Swedish Foundation for Strategic Environmental Research (MISTRA); the Nanoscience and Nanotechnology Area of Advance at Chalmers University of Technology; the Adlerbert Research Foundation; and the Swedish Chemicals Agency (KemI).

Finally, special thanks go to my family and my girlfriend for their ever-present support in life.

Rickard Arvidsson  
Gothenburg, 2012-08-09

“Is it not a strange fate that we should suffer so much fear and doubt for so small a thing?”

Boromir

in *The Fellowship of the Ring* (1954) by J. R. R. Tolkien





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# INTRODUCTION

For a society to be sustainable, “society-produced substances must not systematically accumulate in the ecosphere” (Holmberg et al. 1996). Modern history shows several examples of how emissions of new chemical substances produced in society have violated this principle and caused risks to humans and the environment that were later considered unacceptable. The report *Late lessons from early warnings* describes several cases where scientists issued warnings regarding several such compounds (Harremoës et al. 2001). The examples include the adverse effects of the solvent benzene, human lung damage related to asbestos exposure, ecosystem damage due to bioaccumulation and biomagnification of PCBs, bioaccumulation of the antifouling agent tributyltin, damage to the ozone layer from emissions of halocarbons, and water pollution resulting from the use of methyl tert-butyl ether as an antiknocking agent in gasoline engines. For several of these examples, the adverse environmental and health effects emerged from previously unknown mechanisms, such as the ozone-depleting potential of halocarbons and the ability of lipophilic substances such as PCB and tributyltin to accumulate in living organisms. Endocrine disruptive chemicals are an additional example of chemical substances with adverse effects emerging from previously unknown mechanisms (Colborn and Clement 1992; Colborn et al. 1997; Kortenkamp 2007). The potential of these substances to reduce human fertility and ultimately threaten the survival of humanity was discovered in the 1990s, long after the commercialization of many endocrine disruptive chemicals.

In the 2000s, synthetic, intentionally produced, human-made nanomaterials, henceforth referred to simply as nanomaterials, began to be extensively produced and used. Although some nanomaterials were used as early as the 10<sup>th</sup> century in niche applications, for instance in dye glass and ceramics (Erhardt 2003), the current emerging production of nanomaterials based on more recently acquired knowledge of the physics and chemistry of nanomaterials will result in considerably higher production and use. According to the Project on Emerging Nanotechnologies (2012), the number of consumer products containing nanomaterials is higher than 1000 and is steadily increasing. Discussions of the risks of nanomaterials began in science fiction and popular science literature with stories and discussions about self-replicating nano-robots that could consume all matter on Earth (see, for instance, the books by Drexler (1986) and Crichton (2002)). More mundane risks of nanomaterials were first highlighted in the scientific literature by Colvin (2003) and the Royal Society (2004), and later in a large number of studies. The high surface area of nanomaterials, which follows from their small size, and their unique surface properties have been the major hazardous properties advanced in the literature (Nel et al. 2006; Christian et al. 2008; Handy et al. 2008; Ju-Nam and Lead 2008). Nanomaterials can thus be said to be the newcomer in the family of synthetic substances potentially contributing to the problem of chemical pollution and the violation of the sustainability condition stated by Holmberg et al. (1996). These substances and their risks are studied in this thesis. In particular, this thesis is about the challenges in assessing exposure to nanomaterials.

## 1.1 Research aims

Given the concern that the use of nanomaterials will cause environmental risks, it is important to assess these risks (Colvin 2003; Royal Society 2004; Maynard et al. 2006; Nel et al. 2006; Ju-Nam and Lead 2008). Environmental risks of chemical substances are normally assessed by comparing exposure levels to toxic thresholds for certain organisms of interest (van Leeuwen and Vermeire 2007). It has been suggested that this general approach is also applicable to nanomaterials. There is, however, a wide consensus that current methods of risk assessment may need to be modified when it comes to nanomaterials (Maynard et al. 2006; Owen and Handy 2007; Klaine et al. 2008; Lubick 2008; Wiesner et al. 2009; Abbott and Maynard 2010). In particular, adjustments are needed in regard to exposure assessment, in which data on emissions and the environmental fate of a substance are combined to derive an exposure level. Modifications that have been suggested include the development of new methods for assessing production (Hendren et al. 2011) and emissions (Wiesner et al. 2009) of nanomaterials in a prospective manner (Wiesner et al. 2009) using life cycle approaches (Sweet and Strohm 2006) in addition to new methods for fate modeling based on nanomaterial properties (Handy et al. 2008; Klaine et al. 2008). There were only about ten exposure assessment studies of nanomaterials in 2012, whereas thousands of studies on nanomaterial toxicity already existed in 2008 (Lubick 2008). It is thus clear that exposure assessment research is lagging behind in the area of risk assessment of nanomaterials. Therefore, the main aim of this thesis is

*to contribute to the development of emission and exposure assessment methods in order to enable assessments of the environmental risks of nanomaterials.*

Environmental systems analysis methods are typically developed through an iterative process in which methods are developed and tested for specific cases. In this thesis, different nanomaterials are used in the different cases. Besides being a vital part of the method development, this approach results in case study results on the exposure and risks of specific nanomaterials that are valuable in themselves. Therefore, the secondary aim of this thesis is

*to assess the exposure and risk of specific nanomaterials.*

## 1.2 Research scope

Risk assessment of chemicals is often divided into (1) emission assessment, (2) fate modeling, and (3) effect assessment. In the emission assessment, emissions of the substance of interest are quantified. In fate modeling, the environmental fate of the substance is modeled. In the effect assessment, the toxic effects of the substance are studied for specific organisms in order to derive a safe level or toxic threshold for the substance. The first two parts together

constitute the exposure assessment, in which an exposure level for the substance is derived for specific organisms.

The work conducted within the scope of this thesis is mainly presented in the five papers appended to this thesis. These papers cover different parts of the method of risk assessment of chemicals. In Paper I, challenges in exposure modeling of nanoparticles were outlined and an exposure model for nanoparticles was proposed based on colloidal stability theory. In Paper II, emissions of titanium dioxide nanoparticles were estimated using the method of particle flow analysis. This method was developed in Paper II, starting from the more established method of substance flow analysis, which has previously been used to assess emissions of chemical substances. In Paper III, a similar study to that in Paper II was conducted, but for silver nanoparticles. In Paper IV, a more complete risk assessment of silver (silver nanoparticles and other forms of silver) was conducted for the geographical area of the city of Gothenburg. In Paper V, a review of the environmental and health risks of the nanomaterial graphene was conducted. This study was conducted at a time when few researchers had studied graphene from a risk perspective and thus constitutes one of the first studies of the risks of graphene. Table 1 provides a summary of the five papers. As can be seen, in some papers all parts of a risk assessment of chemicals are included, whereas in some only one or two parts are included.

**Table 1.** Overview of the five papers appended to this thesis. Emission assessment and fate modeling together constitute the exposure assessment.

<b>Paper</b>	<b>Stressors considered</b>	<b>Emissions</b>	<b>Fate</b>	<b>Effects</b>	<b>Journal</b>
Paper I	Titanium dioxide nanoparticles	Included	Included	Not included	Human and Ecological risk Assessment
Paper II	Titanium dioxide nanoparticles	Included	Not included	Not included	Journal of Industrial Ecology
Paper III	Silver nanoparticles	Included	Not included	Not included	Journal of Industrial Ecology
Paper IV	Silver nanoparticles (and other forms of silver)	Included	Included	Included	Human and Ecological Risk Assessment
Paper V	Graphene	Included	Included	Included	Human and Ecological Risk Assessment

The effect assessment part of a risk assessment relies heavily on toxicological and ecotoxicological experimental data. The experimental work has not been part of this thesis, and thus the thesis does not contribute directly to the effect assessment of nanomaterials.

Instead the focus has been on development of exposure assessment methods, which are important given the clear underrepresentation of exposure assessment studies compared to studies on the toxicity of nanomaterials. As can be seen in Table 1, emission assessment and fate modeling, which together constitute the exposure assessment, are more extensively covered than effect assessment. Still, toxic effects of nanomaterials are discussed in Papers IV and V, in which toxicological and ecotoxicological data on graphene, silver and silver nanoparticles are reviewed. In addition, this thesis focuses on risks to the environment rather than human risks, although risks to humans are considered in Paper V.

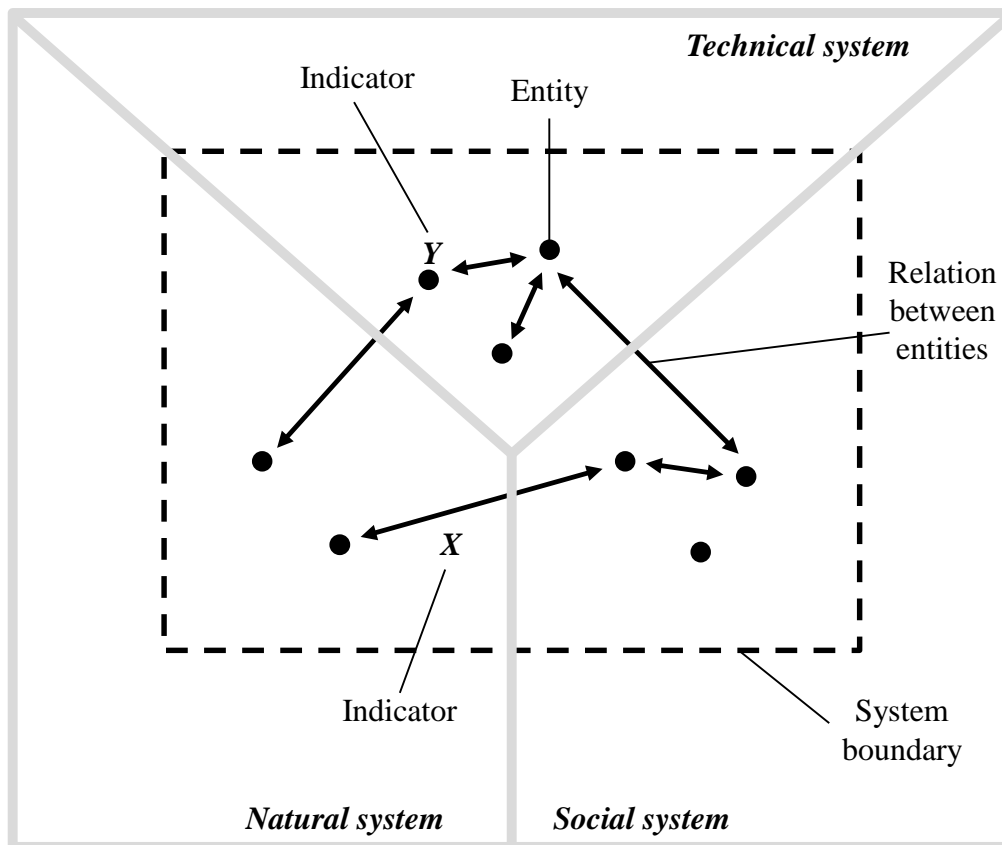
### **1.3 Environmental systems analysis as point of departure**

Systems science has been described as a new paradigm and contrasted with other types of science, such as reductionist natural and social science (Ackoff 1973; Checkland 1993). In systems analysis, scientific knowledge and methods are applied to solve problems or improve situations. Whereas the reductionist approach seeks a deeper level of understanding in the details, systems analysis seeks to provide a holistic perspective on a system related to a problem by developing systems models that include all relevant entities and relations between them. System models are defined by their system boundaries and generally contain different entities that have different relations to each other (Klir 1991; Ingelstam 2002), see Figure 1. The systems approach is particularly useful when dealing with real-world problems that include entities and relations between these entities belonging to the three different general main systems called the social system, the natural system, and the technical system (Miser and Quade 1988a). The development of systems models is often guided by data and theories from the natural or social sciences, but a systems model is mostly developed within a context and in response to a certain problem or issue of interest. Unlike the results from natural science studies, the results from systems analysis models are not always reproducible and cannot always be confirmed by observing the real world (Miser and Quade 1988b). This is due to the uniqueness of some problem situations and the fact that the output of systems models is sometimes abstract and impossible to observe directly. From this, it follows that being “true” or “right” or “correct” may not always be the main goal of a system analysis study, but rather to produce results that are “relevant” for a specific purpose.

The research in this thesis has been conducted within a subfield of systems science, environmental systems analysis, which is systems analysis with the purpose of dealing with environmental problems (Baumann and Tillman 2004). The field of environmental systems analysis contains a number of methods (Baumann and Cowell 1999; Finnveden and Moberg 2005). Two of these have been applied within this work: risk assessment of chemicals and substance flow analysis. They are described in more detail in Sections 2.2 and 2.3. Environmental systems analysis can therefore be said to constitute the foundation or point of departure for this work. Other examples of methods within the field include life cycle assessment, material flow analysis, risk assessment of accidents, environmental impact assessment, and energy analysis (Finnveden and Moberg 2005). Although these environmental systems analysis methods differ in aim and scope, they share important

systemic features. One such feature is the choice of relevant environmental indicators (*X* and *Y* in Figure 1) that should capture important properties of the system studied (Gallopín 1996). Indicators can denote both properties related to entities and properties related to relations between one or several entities. Another shared feature is the explicit definition of the boundaries that delimit the system, while including all relevant aspects of the system in order to enable an environmentally relevant analysis (Lundin et al. 1999). Issues related to model input data, such as data availability, data relevance, and data handling (Suter and Barnthouse 1993; Baumann and Tillman 2004; Zweers and Vermeire 2007; Hillman and Sandén 2008) constitute a third shared feature.

It is worth mentioning that a somewhat unusual kind of quantitative method may be practiced in the field of environmental systems analysis. This method is described by Harte (1988), who argues that it is often sufficient to estimate results within the correct order of magnitude rather than as an exact number in environmental systems modeling. He also argues that, given the problems in obtaining data for environmental system models, an order of magnitude estimate is often the only result that can be obtained with some confidence. Along the same line, Sandén (2008) concluded a discussion of the informational value of environmental assessments of energy technologies with the saying, “it is better to be roughly right than precisely wrong”. As usual, the Greek philosophers had already formulated the principle. Aristotle (350 BCE) said that “it is the mark of an educated man to look for precision in each class of things just so far as the nature of the subject admits”. An alternative translation of this quotation, “it is the mark of an instructed mind to rest easy with the degree of precision which the nature of the subject permits and not seek an exactness where only an approximation of the truth is possible”, has frequently been cited to illustrate the uncertainty that normally surrounds risks related to chemicals (e.g., Cairns and Cherry (1983) and van Leeuwen and Vermeire (2007)).



**Figure 1.** A general illustration of a system model, inspired by illustrations by Ingelstam (2002) and Baumann and Tillman (2004).

## 1.4 Research method

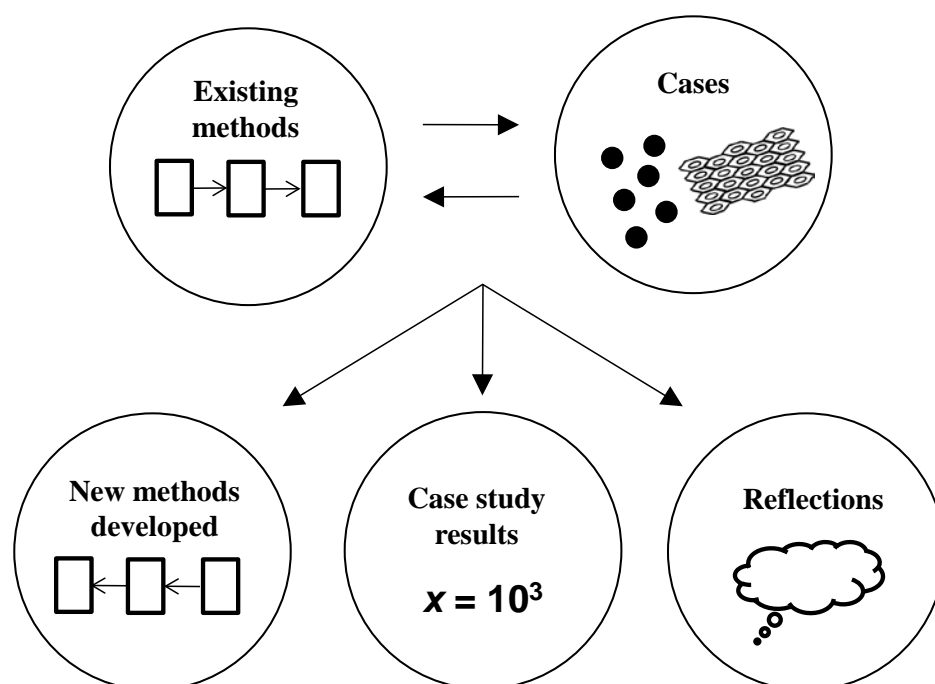
This work has been an iterative process of developing methods and testing them on specific cases. This process of method development through case studies is typical of systems analysis (Miser and Quade 1985), similar to the abductive logic-based systematic combining approach described by Dubois and Gadde (2002). In addition to being a way to develop new methods, such method-case-method iterations also provide specific case study results. Figure 2 describes schematically how existing environmental systems analysis methods were modified through case studies during this work, resulting in new methods and also in specific case study results and more abstract reflections.

The main method used has been risk assessment of chemicals, which has long been used to assess the environmental impact of chemicals with regards to their toxic effects (Suter 1993c; van Leeuwen and Vermeire 2007). However, for assessing emissions, substance flow analysis was a complementary method of departure in Paper II and III. Substance flow analysis can be used to estimate emissions of a substance, thus constituting the emission assessment of a risk assessment (van der Voet et al. 1999). Risk assessment of chemicals and substance flow analysis are unique among environmental systems analysis methods in that they are the only



methods focusing on chemical substances as the unit of analysis (Finnveden and Moberg 2005).

Life cycle assessment is another environmental assessment method that has been used to assess the environmental impact of nanomaterials (Kushnir and Sandén 2008; Grubb and Bakshi 2011). However, although the energy used and emissions caused during the life cycle of nanomaterials constitute interesting research topics, the main environmental concern regarding nanomaterials has been their potential toxic effects on humans and other organisms (Colvin 2003; Royal Society 2004; Maynard et al. 2006; Nel et al. 2006; Ju-Nam and Lead 2008). Life cycle assessment is also primarily aimed at assessing the environmental impacts of products and not specific substances contained within products (Baumann and Tillman 2004). There has been considerable difficulty in including the toxic impact of chemicals into the life cycle assessment method (Finnveden et al. 2009). This is mainly due to the lack of spatial, temporal, dose-response, and threshold information in life cycle assessment, which is dealt with by simplifying assumptions. It has been suggested that these simplifications have resulted in unrealistic worst-case estimates of the impact of chemical substances (Owens 1997). As noted by Curran et al. (2007), including the impact of nanomaterials in the life cycle assessment method may prove an even greater challenge than including chemical substances.



**Figure 2.** The work described in this thesis has been an iterative process based on the methods of risk assessment of chemicals, substance flow analysis, and case studies of specific nanomaterials (titanium dioxide nanoparticles, silver nanoparticles, and graphene). The outcomes are in the form of new methods, case study results, and reflections.

## 1.5 Case study stressors

A number of nanomaterials have already been the subject of risk-related studies, including nanoparticles of titanium dioxide, silver, zinc oxide, cerium dioxide, iron, and fullerenes, as well as carbon nanotubes. More details will be provided in Chapter 4. The nanomaterials studied in this thesis are titanium dioxide nanoparticles, silver nanoparticles, and graphene. Titanium dioxide nanoparticles were chosen because an early risk assessment study indicated higher risks for this nanomaterial than for the others in that study (Mueller and Nowack 2008). Silver nanoparticles were chosen because it is the nanomaterial presumed to be most widely used in consumer products (Project on Emerging Nanotechnologies 2012). Several studies have raised concerns about the potential risks of silver nanoparticles and recommended additional studies (Blaser et al. 2008; Luoma 2008; Wijnhoven et al. 2009). Silver is also a substance that has caused environmental problems before (Luoma 2008). Unlike titanium dioxide and silver nanoparticles, which are already present in consumer products, graphene has only recently begun to be commercialized and produced on a large scale (Segal 2009). Graphene has not yet been extensively studied from a risk perspective; in fact, the focus of the discussion of nanomaterial risks has mainly been on *particulate* materials, while graphene is a sheet that is constrained to a few nanometers in one dimension only. Graphene is therefore included in order to apply and develop risk assessment and substance flow analysis methods for a less studied, non-particulate nanomaterial.

# 1 ASSESSING RISK

The concept of risk has been discussed in various scientific contexts and there is no commonly accepted definition (Renn 1998). The definitions vary depending on the scientific discipline (e.g., engineering or social sciences) and the risks considered (e.g., financial, human health, or environmental). It is thus important to be clear about how the term is used in specific contexts (Renn 1998). A number of different definitions and theories of risk can be found within the social sciences. These typically focus on how risks are perceived by people rather than quantitative assessments of risk. To elaborate on all of those definitions and theories is beyond the scope of this thesis. Examples of such social science definitions and theories of risk include the cultural theory of risk (Thompson et al. 1990), the risk society concept (Beck 1992b; Beck 1992a), the risk compensation concept (Adams 1995), psychometric measurements of risk perception (Slovic 2000), the relational theory of risk (Boholm and Corvellec 2010), and many more. Some of those social science studies criticize quantitative risk assessments. Instead, some social scientists highlight the importance of risk perception, risk communication, and the public understanding of risk (Renn 1998). Although risk perception, communication, and the public understanding of risk are certainly important, quantitative measures of risk are useful in decision-making processes, not least for comparing and prioritizing different risks (Kaplan and Garrick 1981; Suter 1993a). Social scientists studying risk have also admitted the usefulness of quantitative assessments of risk (Renn 1998; Slovic 2002).

## 1.1 Risk definitions

In technical contexts, risk is often defined as a combination of probability and consequence, and can be calculated according to this definition. A general way of expressing risk according to this definition is provided by Kaplan and Garrick (1981):

$$R = \{S, P, C\} \tag{1}$$

where  $R$  is the risk,  $S$  is a certain scenario,  $P$  the probability of that scenario and  $C$  the consequence of the scenario. When operationalizing Eq. 1 for the purpose of risk assessment, it can be reformulated into the general equation:

$$R = f(P, C) \tag{2}$$

More specific operationalization of Eq. 2 can be found, such as assessing risk as the product of the probability and consequence of a certain adverse event (Kaplan and Garrick 1981; Lindhe et al. 2009). Note, however, that the operationalization of Eq. 2 requires a definition of the scenario  $S$  in order for  $P$  and  $C$ , and consequently  $R$ , to be meaningful. The definition of risk in Eq. 1 and 2 is often used for assessing technical risks (Renn 1998). In risk assessment

of chemicals and ecological risk assessment, the definition of risk according to Eq. 1 and 2 is not always the most relevant approach. This is because such probabilistic risk assessment is based on binary logic, meaning that only two conditions are possible (Bedford and Cooke 2001). For example, the machine may be broken or not broken; in other words, it belongs to the binary set of {broken, not broken}. For the case of organisms exposed to chemicals, the exposure represents an infinite range of possible conditions, such as 1 mg/kg body weight, 2 mg/kg, 3 mg/kg, 3.7 mg/kg, and so on. Exposure thus does not belong to a binary set, but rather to the infinite set of real numbers  $\{\mathfrak{R}\}$ . The interesting question from a chemical and ecological risk perspective is thus not so much whether exposure occurs, but rather whether the exposure is high enough to cause adverse effects and what these effects are. When assessing the risks of chemical substances, it is thus more relevant to relate exposure of a substance to some sort of threshold based on toxic effects, which is a definition of risk different from the probability-and-consequence type definition in Eq. 1 and 2 (Kaplan and Garrick 1981; Burgman 2005). By analogy to Eq. 2, this definition can be expressed mathematically:

$$R = f(\text{exposure, effects}) \quad (3)$$

This definition of risk is often used in ecological risk assessment and risk assessment of chemicals and is operationalized in terms of risk quotients (RQs) (Suter 1993a; van Leeuwen and Vermeire 2007), which are estimated as follows:

$$RQ = \frac{PEC}{PNEC} \quad (4)$$

where PEC stands for predicted environmental concentration and PNEC for predicted no-effect concentration. Both PEC and PNEC are generally measured as mass concentrations, for example in units of mg/l. Note that, as in Eq. 2, the input parameters in Eq. 4 (PEC and PNEC) must be defined for the specific situation. For example, the PEC can be related to a specific environmental compartment of interest (e.g., soil, water, air, or sediment) and different exposure pathways (e.g., inhalation, ingestion, or dermal contact). PNEC may refer to different organisms in that compartment. The definition of risk according to Eq. 4 is generally applied throughout the work in this thesis, although, as discussed later, mass concentration is not always used as a unit for PEC and PNEC when nanomaterials are involved. The general idea of comparing an exposure level to thresholds is applied in many risk regulation contexts. In such specific contexts, terms other than PEC and PNEC may be used. For risks to humans, predicted daily intake may be used instead of PEC, and acceptable daily intake or guideline value instead of PNEC.

One concept that is related to risk is hazard. For technical risks, when risk is a function of probability and consequence, hazard is defined as “a situation that in a particular circumstance could lead to harm” (Burgman 2005). In other words, a situation has a known possible

adverse consequence, but the probability of that consequence actually occurring is unknown. Kaplan and Garrick (1981) expressed this mathematically as follows:

$$R = \{S, C\} \quad (5)$$

This is the same expression as Eq. 1 but without the probability  $P$ . For chemical risks, where risk is a function of exposure and effects, a hazard is “the inherent capacity of a chemical or mixture to cause adverse effects in man or the environment under the conditions of exposure” (van Leeuwen and Vermeire 2007) or “the potential for exposure of organisms to chemicals at potentially toxic concentrations” (Suter 1993a). In other words, a chemical hazard is a chemical that has the potential to cause risk due to one or several of its properties, such as high toxicity and persistence. Such properties can be related to both exposure and effects, that is, to both PEC and PNEC. Eq. 3 thus applies to both chemical risk and hazard. However, in the case of hazard, exposure and effects are not calculated but rather based on known chemical properties.

## 1.2 Risk assessment of chemicals

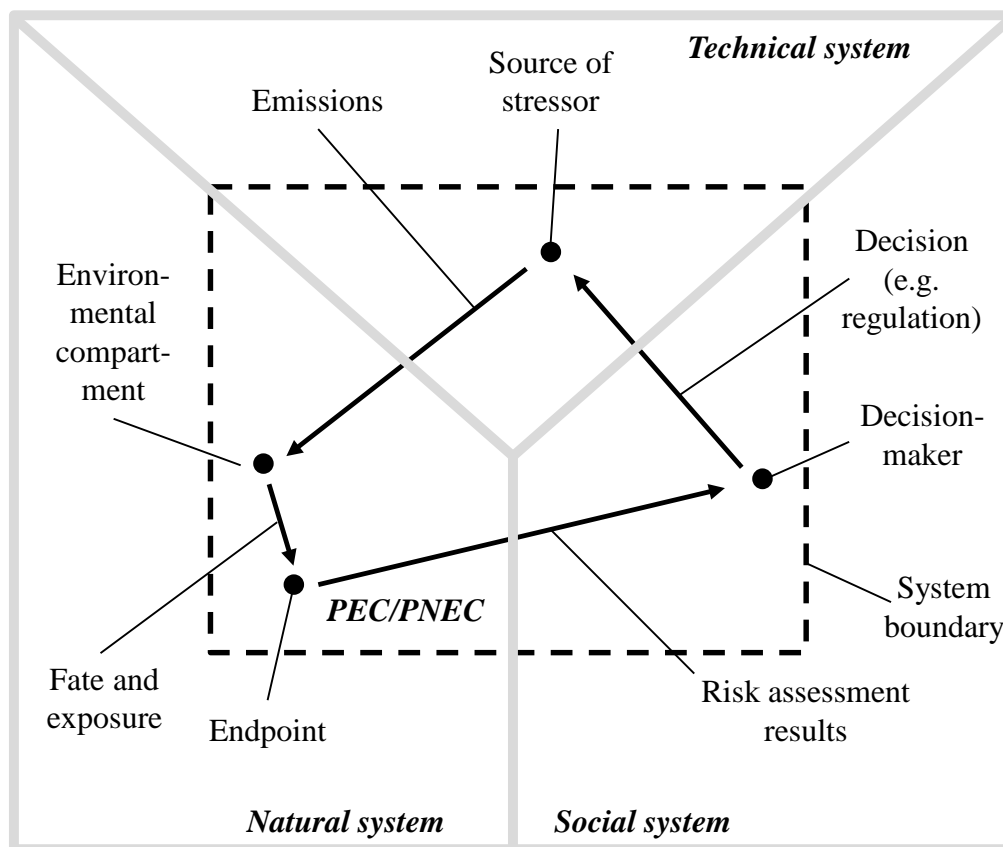
Historically, humans have been the primary focus of risk assessments, but as environmental problems have become more obvious, risks to the environment have been more frequently considered. Environmentally related risk assessments are rooted in early calls for environmental protection, such as those by Carson (1962) in her book *Silent Spring*. The development of methods for environmentally related risk assessment has largely been a joint discussion between scientists and different national and international governmental bodies, such as the Organization for Economic Co-operation and Development (OECD), the World Health Organization (WHO), the United States Environmental Protection Agency (USEPA) and the European Commission (Suter 1993a; van Leeuwen and Vermeire 2007). Assessing the risks of chemicals was also recommended as a vital part of environmentally sound management of chemicals within Agenda 21 (United Nations 1992). There are a number of slightly different environmentally related risk assessment methods. Their primary focus has been on assessing risks related to chemicals, although risks from other stressors may also be assessed (Suter 1993a). Examples of specific environmentally related risk assessment methods include risk assessment of chemicals (van Leeuwen and Vermeire 2007) and ecological risk assessment (Suter 1993a; USEPA 1998). Ecological risk assessment often has a stronger focus on the endpoint, whereas the risk assessment of chemicals is more focused on the stressor. The endpoint (sometimes called the receptor) is a representation of the value that the risk assessment aims at protecting (Suter 1989), typically an organism. The stressor is something that threatens the endpoint; typically a chemical substance in environmentally related assessments.

The aim of risk assessment of chemicals is to provide early warning signals regarding any adverse effects that may not be obvious to an unskilled observer, thus informing

environmental decision-making (Renn 1998). Risk assessment of chemicals allows for predictive assessments of the consequences of additional emissions and of risk mitigation measures. Natural systems are often slow to respond – for example, the residence time of persistent pollutants can be decades or longer in aquatic compartments – and it is hence impossible to explore and compare increases in emissions or risk mitigation measures experimentally in the real world. Risk assessment of chemicals provides valuable guidance here. It has been a major scientific and regulatory method for management of chemical risks (Côté and Wells 1991). This method is also currently applied in the risk assessments of chemicals conducted within the European legislation on Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) (European Chemicals Agency 2011).

The source-fate-endpoint cause-effect chain (Figure 3) is central to risk assessment of chemicals and other environmentally related risk assessments. The origin of the stressor is denoted as the source, which can be a chemical factory or a product containing the stressor. The stressor can reach the endpoint and cause exposure during its environmental fate. Bioaccumulation through the food web is a typical fate mechanism of environmental toxins that can lead to human exposure. In Figure 3, part of the social system is also included. Indeed, the interpretation of risk assessment results and the decisions taken by decision-makers to reduce or not reduce risk lies within the social system. These processes are, however, not part of risk *assessment*, but rather risk *management* (Patton 1993).

The method of risk assessment of chemicals can be said to consist of four steps (van Leeuwen and Vermeire 2007). The first step is hazard identification, in which potential hazards such as the use of chemicals known to be toxic are identified. A source-fate-endpoint model, sometimes referred to as source-pathway-receptor model, is developed. Such a model includes identifying the source, stressor, environmental fate, and endpoints. Risk assessments of chemicals can vary in scope and scale (Patton 1993), and this will affect the source-fate-endpoint model. Ideally, the choice of sources, stressors, environmental fate mechanisms, and endpoints should be coordinated to ensure the combined relevance of the source-fate-receptor cause-effect chain (Suter 1993c). Defining the endpoint for the purpose of risk assessment is particularly challenging. Suggested criteria for choosing relevant endpoints include societal relevance, biological relevance, unambiguous operational definition, accessibility to prediction, measurement, and susceptibility to the stressor(s) of interest (Suter and Barnthouse 1993).



**Figure 3.** A source-fate-endpoint cause-effect chain describing the system considered in a risk assessment of chemicals. The figure is analogous to the more general Figure 1. Note that the part of the system that lies within the social system in this figure is not actually a part of risk *assessment*, but rather risk *management* (Patton 1993).

The second step in a risk assessment of chemicals is called exposure assessment. The word “exposure” is defined as concentration or amount of a particular stressor that reaches a target individual or population at a specific frequency for a defined duration (van Leeuwen and Vermeire 2007). Exposure is thus the tempo-spatial coincidence of stressor and endpoint. One may differentiate between internal and external exposure, where internal exposure refers to the dose absorbed or delivered to the whole individual or particular organs, and external exposure to the concentration present in the direct proximity of the individual (Suter 1993b). For practical reasons, external exposure is more often considered, although it can be used to estimate an internal exposure based on toxico-kinetic models. External environmental exposure is typically quantified in terms of the predicted environmental concentration (PEC). Often different environmental compartments (water, air, soil, and sediment) are considered, and PECs are calculated for each of them. In order to derive a PEC, both an assessment of the emissions of the stressor and environmental modeling of its subsequent fate are required. Deriving a relevant PEC is not a trivial matter since exposure varies with time and safety measures taken.

Since the 1990s, exposure assessments of chemicals have to a large extent relied on multi-compartment mass-balance models and steady state, based on the work of Mackay et al. (1991; 1992; 1996). The principal idea is to divide the environment into well-mixed, homogeneous boxes, each one representing the major environmental compartments, that is, soil, sediment, water, and air (van de Meent and Bruijn 2007). In the basic models, each compartment is assumed to be in a steady state with its neighboring compartments; the system is closed and, in its simplest form, losses due to biodegradation or abiotic degradation are ignored. Mass-balance equations based on the physico-chemical properties of a chemical are then employed to calculate its expected distribution in the model system. More advanced, higher tier models can include systems in a non-steady state and can include continuous or fluctuating emission and loss functions such as biodegradation. Such exposure models enable assessment of the relative importance of different processes for the fate of the contaminant (Williams et al. 1999) and allow for sensitivity analyses in order to identify the critical factors for the output of the model. Further division of the major compartments into sub-compartments may also be conducted. This can show which environmental compartments may be expected to contain the highest PEC and which concentrations occur on different spatial scales.

Multi-compartment mass-balance models are still used and considered useful today (MacLeod et al. 2010). Other approaches to spatially explicit multi-compartment models have also been attempted, such as using geographic information systems (GIS) for modeling of chemical fate (Pistocchi et al. 2010).

The purpose of the third part of a chemical risk assessment, denoted the effect assessment and sometimes referred to as a dose-response assessment, is to attempt to quantify effects for risk assessment purposes. Effects are defined as changes in an individual or population caused by exposure to a stressor (van Leeuwen and Vermeire 2007). Organisms in the environment may experience a number of different adverse effects due to exposure to chemicals, including reduction of survival, growth and reproduction; increased levels of avoidance; and increased deformities or tumors (Stephan 1986). Different species may exhibit very different sensitivities to a specific stressor. In fact, due to differences in consumption patterns, local abiotic factors, exposure time, surface area/volume ratio, life histories, and behavior, even specific individuals within species may exhibit different sensitivities to a stressor (Traas and van Leeuwen 2007). In the effect assessment, toxicological and ecotoxicological data are applied to determine the highest dose or concentration at which there will be no adverse effects to a certain endpoint. This concentration is referred to as the predicted no-effect concentration (PNEC) and is ideally derived from dose-response curves (Traas and van Leeuwen 2007). In practice, dose-response curves are not always available for the stressor and endpoint of interest. For those cases, PNEC values can be derived based on the concentration at which a certain fraction of the exposed population died ( $LC_x$ , where L stands for lethal, C for concentration and  $x$  represents the fraction that died), the concentration at which it was possible to see an effect on a fraction of the organisms tested ( $EC_x$ , where E stands for effect, C for concentration and  $x$  for the fraction for which an effect could be seen) or the highest concentration that had no statistically significant adverse effects on the exposed endpoints

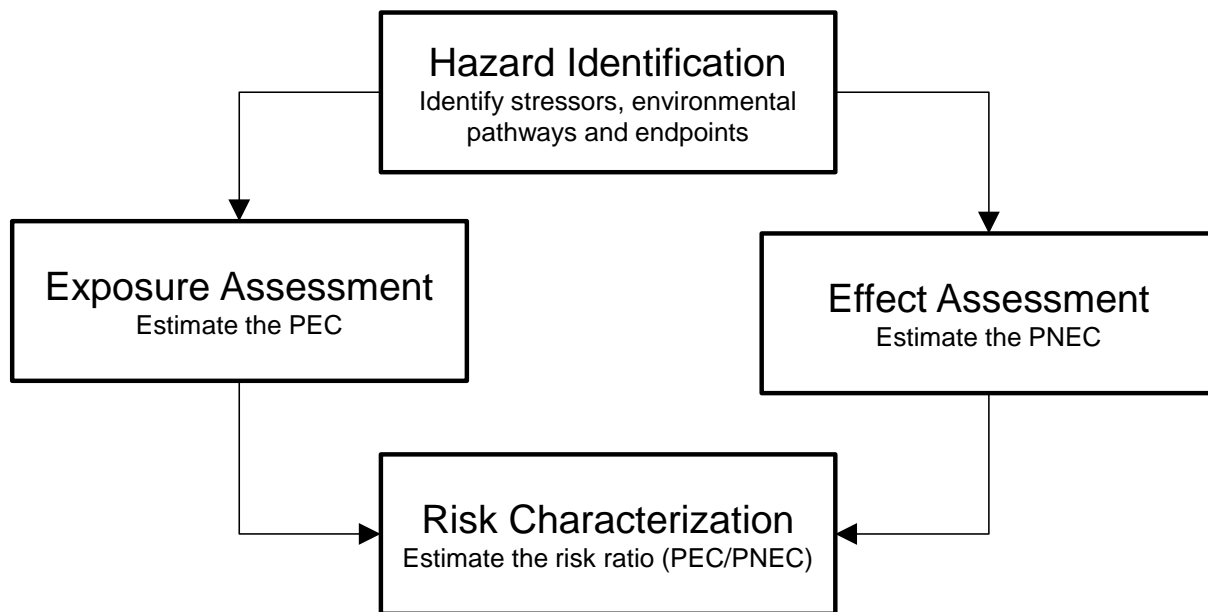


compared to the controls, denoted the no-observed-effect concentration (NOEC). These concentrations must then be divided by an assessment factor that varies between 10 and 10 000, depending on available data in order to obtain a PNEC. The assessment factor may also be referred to as the uncertainty factor or the application factor. Assessment factors are not based on mechanistic models but rather on experience from effect assessment (Traas and van Leeuwen 2007). The use of assessment factors has been criticized as lacking scientific basis (Allard et al. 2010). The use of NOEC values has also been criticized for being simplistic and unscientific (Jager 2012). Still, deriving relevant PNEC values is a vital part of risk assessment of chemicals, and sometimes NOEC values and application factors are the only available ways to do so.

Although there is always a possibility that other species and individuals in the ecosystem are more sensitive than the ones for which ecotoxicological data exist, in practice, it is typically assumed that the protection of the species and individuals of an ecosystem is ensured by deriving PNEC values based on the ecotoxicological data that indicates the highest toxicity and by applying assessment factors (Traas and van Leeuwen 2007). An alternative method for deriving PNEC values to ensure low risk to ecosystems is through species sensitivity distributions, in which ecotoxicological data from a number of different species are combined in order to derive a PNEC value (Posthuma et al. 2002). The drawback to this method is that it requires numerous ecotoxicological datasets that may not always be available.

In the fourth and last part of a risk assessment of chemicals, called risk characterization, the PEC and PNEC are compared according to Eq. 4. If the PEC is higher than the PNEC, that is, if the quotient  $PEC/PNEC$  is higher than one, it indicates risk. The PEC and PNEC may also be expressed not as single numbers but as ranges or even probability distributions in order to conduct a more detailed risk characterization.

It should be noted that in risk assessment of chemicals, normally the risk of one substance alone is assessed. There is, however, growing concern regarding the potential risks of mixtures of chemical substances. Although some progress has been made in this area, this is still an emerging research field (Kortenkamp et al. 2009). The risks related to mixtures of different nanomaterials, or mixtures of nanomaterials and “ordinary” chemical substances, have not been considered in this thesis.



**Figure 4.** The method of risk assessment of chemicals, modified from van Leeuwen and Vermeire (2007).

### 1.3 Substance flow analysis

As noted in Section 2.2, assessing emissions is a vital part of a risk assessment of chemicals. Substance flow analysis is sometimes applied prior to the risk assessment in order to estimate emissions (van der Voet et al. 1999). As with risk assessment of chemicals, the focus of a substance flow analysis is a substance of interest, often a substance that either causes adverse environmental impacts when emitted, or is a scarce substance, or both. Substance flow analysis is an established method in the field of industrial ecology (van der Voet 2002), and is based on the law of mass conservation first developed by Lavoisier (1789):

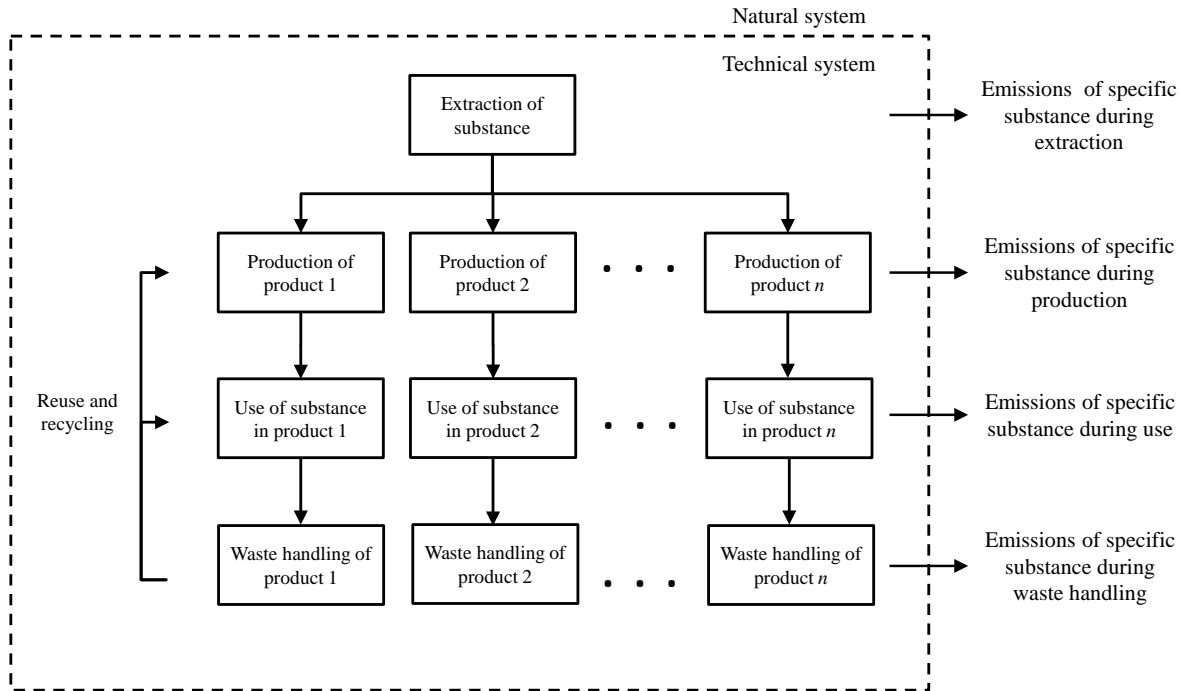
$$\frac{dm}{dt} = \sum \dot{m}_{in} - \sum \dot{m}_{out} \quad (6)$$

where  $\dot{m}$  represents mass flows to and from a certain process and  $m$  represents the mass stock of the process. The purpose of a substance flow analysis is to quantify flows and stocks of the substance of interest to society. The analysis is often based on product life cycles, that is, raw material extraction, production, use, and waste handling. Flows between and stocks within these different life cycle stages are quantified. Of course, the products included in the analysis are products in which the substance of interest is a constituent. Flows are often measured as mass per unit time, for instance as metric tonnes/year, and stocks are measured as mass only, for instance tonnes. Emissions from society to the environment are of specific interest in many substance flow analysis studies since these flows are of particular environmental importance. Figure 5 shows a generic illustration of a substance flow analysis model. Substance flow analysis studies are conducted for specific substances, and also often for

specific regions. Examples of substances and regions investigated include metals such as mercury in the United States (Cain et al. 2007) and cadmium in Australia (Kwonpongsagoon et al. 2007); nutrients such as phosphorous (Brunner 2010); and organic chemicals such as parabenes in Denmark (Eriksson et al. 2008).

Material flow analysis (Bringezu and Moriguchi 2002) is similar to substance flow analysis. Although the difference between these two methods is not always clear-cut, materials flow analysis focuses not on individual chemicals, but on materials which can consist of several different chemical substances. Examples of materials considered in materials flow analysis studies are computer waste (Steubing et al. 2010) and paper (Hong et al. 2011). It is, however, possible to find studies called material flow analysis that study flows and stock of a single chemical substance, such as the so-called material flow analysis of phosphorus by Qiao et al. (2011). According to the definitions above, this would be classified as substance flow analysis. Sometimes the two concepts are used synonymously in the same study, as in the substance/material flow analysis of cement by Kapur et al. (2008), which would be classified as a material flow analysis according to the definitions presented here. However, substance flow analysis can also be seen as a sub-category of material flow analysis (Bringezu and Moriguchi 2002), which would allow a wider use of the term “material flow analysis”.

The work on biogeochemical cycles (Lenikan and Fletcher 1977; Smil 1985; Schlesinger 1991) can be seen as a precursor of both substance and material flow analysis (van der Voet 2002). Important steps towards harmonizing substance and material flow analysis were taken in the 1990s by, for example, Baccini and Brunner (1991), Ayres and Simonis (1994), Adriaanse et al. (1997) and Bringezu et al. (1998).



**Figure 5.** A substance flow analysis model.

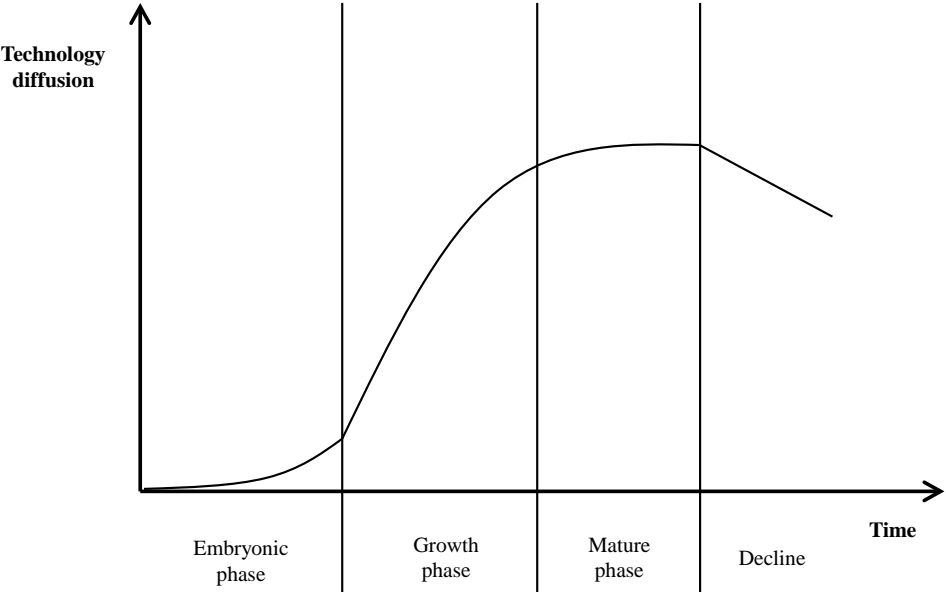
## 1.4 Risk assessment and technological change

A broader perspective on risk assessment of chemicals can be gained by relating it to technological change. It is one of the environmental assessment methods that can be used to guide technology choices in society. Nanomaterials bring both promises of technological solutions and concern for potential risks (Royal Society 2004). The challenge for society is largely to determine which nanomaterials bring mostly promise and which bring mostly risk. One proposed way of dealing with this situation is reflexive innovation, which evaluates risks simultaneously with technological development in a reflexive way that enables society to avoid severe negative side-effects from technologies (Fogelberg and Sandén 2008). The question is how to assess the risks of emerging technologies such as nanomaterials so as to allow society to avoid those that cause severe risks (Wiesner et al. 2009).

Technologies do not remain constant over time; they generally undergo changes over their life cycle (Grübler and Nakićenović 1991; Grübler 1996). The technological life cycle can be illustrated by a graph, where technology diffusion is plotted against time (Figure 6). Such a graph generally shows four distinct phases. The first phase has been termed the embryonic phase, introduction, childhood, or formative phase. It is characterized by high uncertainty and much competition between diverse designs. The second phase is called the growth phase, adolescence, or the diffusion phase. This phase is characterized by rapid technology diffusion. During this phase, the varying designs characterizing the embryonic phase tend to decrease in number, and a dominant design may emerge (Abernathy and Utterback 1978). This dominant design then takes root. Machines adapted to this specific design may be produced, and people may receive training related to the dominant design. An example of a dominant design is the QWERTY keyboard, used for computer and typewriter keyboards in many countries (David 1985). Initially developed to slow down typewriting so as to avoid the type bars clashing, people were trained to use it and became accustomed to it. Today the QWERTY keyboard has been adopted for computer keyboards even though they have no type bars. The third phase is called the saturation or mature phase. In this phase, growth rates slow down due to diminishing returns. Technologies may also eventually face decline, which is the fourth and last phase of the technological life cycle.

In this lies a dilemma, denoted the Collingridge dilemma after Collingridge (1980). When technologies have reached the mature phase and have perhaps become dominant designs, they are difficult to change or constrain in response to risks to the environment or to human health. This indicates the importance of trying to assess risks related to technology as early as possible in technological development, in line with reflexive innovation systems thinking. However, in the embryonic phase of the technological life cycle, technologies are immature and characterized by competing designs, and it is difficult to know which risks may arise from the technologies if and when they reach the mature phase. Examples of this dilemma include gasoline and diesel as fuels. It would have been easier to constrain their use in the early 1900s, but the environmental risks of gasoline and diesel (e.g., emissions of the greenhouse

gas carbon dioxide) were not known at that time. Collingridge (1980) himself suggested that future states of the technology should be considered and preferably forecasted, and then be subjected to various assessments. However, he also acknowledged the difficulty of gaining legitimacy for an assessment based on a view of the future state of a technology in light of the difficulties of forecasting technological change. To date, no harmonized method for assessing risks of emerging technologies exists.



**Figure 6.** Illustration of a stylized technological life cycle, modified from Gröbler (1998).

## 2 NANOMATERIALS

Although he did not explicitly use the term “nanomaterial”, nanomaterials were first mentioned in the presentation “There is Plenty of Room at the Bottom” by Richard P. Feynman in 1959, where he addressed the possibilities of manipulating single atoms as a more powerful form of synthetic chemistry. The term “nano”, as in nanotechnology and nanomaterials, was first used by Norio Taniguchi in 1974, when he stated that: “Nanotechnology mainly consists of the processing of, separation, consolidation, and deformation of materials by one atom or one molecule.”

Since then, the production of nanomaterials has exploded. A list of products that their producers claim contain nanomaterials can be found in the database provided by the Project on Emerging Nanotechnologies (2012). The number of products included in this database was higher than 1000 in 2012. Examples of nanomaterials that are produced today include nanomaterials from titanium dioxide, silver, iron and zinc oxide, as well as carbon nanotubes and graphene. Titanium dioxide nanomaterials are used for their photocatalytic properties. These properties can be utilized in self-cleaning windows (Sanderson et al. 2003) and self-cleaning cement (Cassar et al. 2003). Titanium dioxide nanoparticles are also used in sunscreen to block and absorb UV light (Nohynek et al. 2007; Serpone et al. 2007; González et al. 2008). Silver nanomaterials are the most frequently occurring nanomaterials in the Project on Emerging Nanotechnologies (2012), and are found in about one fifth of the products. They are primarily used for their antibacterial properties in consumer products and wound dressings (Brett 2006; Silver et al. 2006; Luoma 2008; Wijnhoven et al. 2009). Iron nanoparticles can be used for soil remediation (Schmidt 2007). Zinc oxide nanoparticles are also used in sunscreen (González et al. 2008). Carbon nanotubes have potential uses in a number of products (Kohler et al. 2008). Graphene is beginning to be produced on a large scale with potential applications in composites and electronics (Segal 2009). Most of these nanomaterials are currently in the embryonic phase, although some, such as silver nanoparticles for antibacterial purposes and titanium dioxide nanoparticles in sunscreen, may already have entered the growth phase.

### 2.1 Nanomaterial definitions

A number of attempts have been made to define nanomaterials to differentiate them from other chemical substances. Often, nanomaterials are defined by a size range limited by at least one of the dimensions. This range may be 1–100 nm (British Standards Institution 2007; ISO 2008), 0.1–100 nm (Royal Society 2004), less than 100 nm (O'Brien and Cummins 2008), or less than 500 nm (Handy et al. 2008). The most common and accepted definition is probably the 1–100 nm range. In addition, it is sometimes suggested that to be counted as a nanomaterial the material must have properties different from those of the bulk form of the same chemical substance (Foss Hansen et al. 2007). A more detailed review of different

definitions of nanomaterials, especially from a regulatory point of view, has been conducted by Lövestam et al. (2010).

The European Commission recently released their suggested definition of nanomaterials: “‘Nanomaterial’ means a natural, incidental or manufactured material containing particles, in an unbound state or as an aggregate or as an agglomerate and where, for 50% or more of the particles in the number size distribution, one or more external dimensions is in the size range 1 nm–100 nm” (European Commission 2011).

It has also been suggested that defining nanomaterials is neither feasible nor necessary. Maynard (2011) writes that the existing definitions lack scientific justification. He argues that instead of trying to establish a definition of nanomaterials suitable for all cases, the focus should be on the novel properties and phenomena associated with specific nanomaterials.

## **2.2 Nanomaterial typologies**

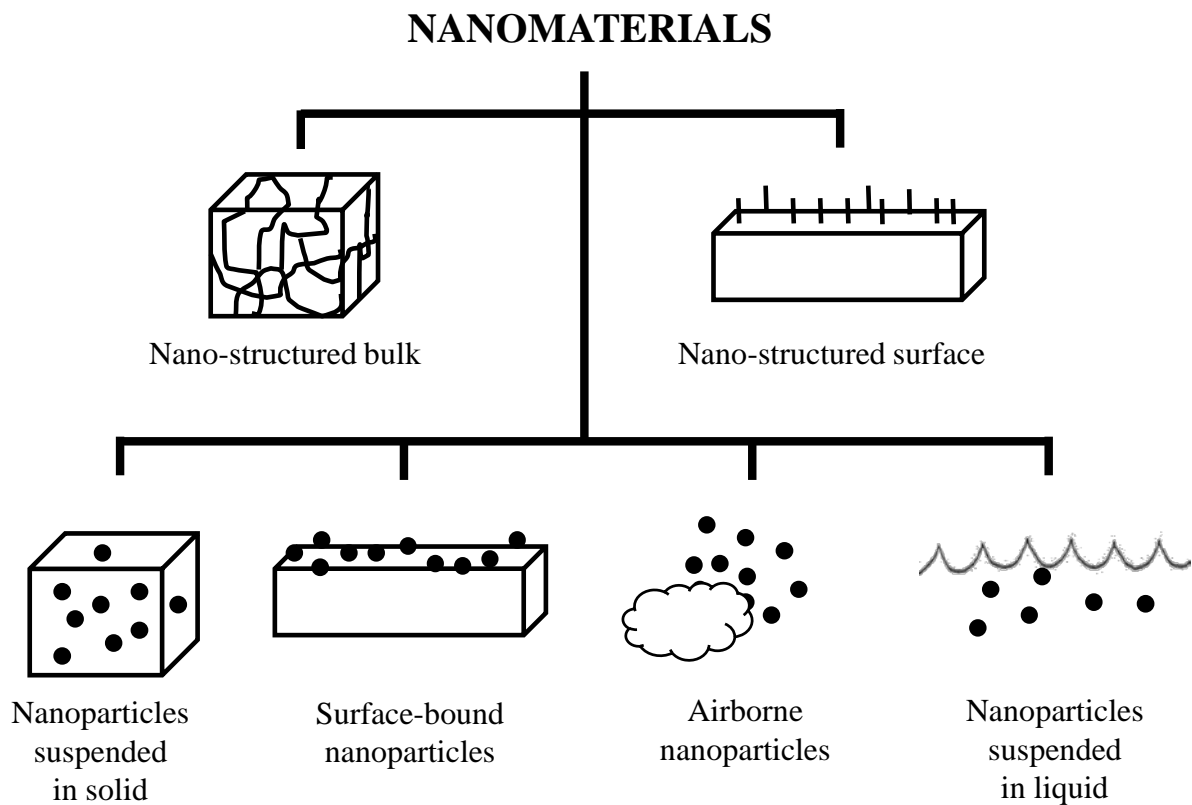
A number of efforts have been made to categorize nanomaterials into different typologies. One approach uses the typology developed by Foss Hansen et al. (2007), which is based on physical shape. It includes three main categories, which are (1) bulk nanomaterials, (2) nanomaterials that constitute surfaces, and (3) nanoparticles (Figure 7). The nanoparticles can be in several forms, such as airborne, surface-bound, or suspended in a liquid or a solid. Jiang et al. (2009) present a more detailed typology for nanoparticles specifically, which includes free particles, agglomerates held together by van der Waals bonds, and aggregates (or sintered particles) held together by covalent bonds.

Another way to categorize nanomaterials, particularly nanoparticles, is based on their chemical composition. An often-used typology is (1) carbon nanomaterials, such as fullerenes and carbon nanotubes, (2) metal oxide nanoparticles, such as titanium dioxide and zinc oxide, (3) metal nanoparticles, such as silver and iron nanoparticles, (4) others, such as quantum dots and nanopolymers (Ju-Nam and Lead 2008; Ma et al. 2010).

Some authors have developed typologies based on the complexity of the nanomaterials. Tour (2007) argues that there is a shift from passive nanotechnology towards active nanotechnology. He defines passive nanotechnology as materials where “the nano part does nothing particularly elaborate”. This category includes the nanomaterials described above, that is, titanium dioxide, silver, iron and zinc oxide nanoparticles, as well as carbon nanotubes and graphene. Active nanotechnology, on the other hand, is characterized by “the nano entity doing something elaborate such as absorbing a photon and releasing an electron, thereby driving the device”. Current examples of this category are not as numerous, but Tour (2007) gives as an example complex molecules called “nano cars” that can move on a surface and move differently depending of their specific design. In addition, Tour (2007) defines a third category, lingering somewhere between passive and active nanotechnology. This category is

referred to as hybrid nanotechnology, where the nano part has some task to perform but “the platform carries the bulk of the burden”. However, the author himself states that this category can be difficult to distinguish from the other two.

A similar typology was developed by Roco (2004), who defined four different kinds of nanostructures. The first two are called passive and active, and correspond to the two presented by Tour (2007). Besides these, Roco (2004) added two further categories: 3D nanosystems and systems of nanosystems, and heterogeneous molecular nanosystems. The first refers to the shift into heterogeneous nanostructures, and the second to structures where each molecule in the system has a specific structure and plays a different role, similar to biological enzymatic systems. These two last categories can be seen as a continuation of the active nanostructure and are somewhat difficult to distinguish from other active nanostructures (Davies 2009). Subramanian et al. (2010) suggested, based on a bibliometric analysis, that there are indeed indications of a shift towards more active nanomaterials.



**Figure 7.** Typology for nanomaterials based on physical shape, modified from Foss Hansen et al. (2007).



### **3 REVIEW OF EXPOSURE AND RISK ASSESSMENTS OF NANOMATERIALS**

A review of the work conducted so far by other authors on exposure and risk assessment of nanomaterials is presented as a background. The currently known exposure and risk assessment approaches for nanomaterials were reviewed and compared. Only studies performing exposure or risk assessments of nanomaterials, or proposing exposure or risk assessment methods, have been included. However, studies in which the (eco)toxicity of specific nanomaterials or nanomaterials is only discussed in general are not included. In addition, studies in which the risks of nanomaterials are discussed in general, in a review-like fashion, have not been included.

This review is focused on method and not on the results of the studies. Some assessment results for titanium dioxide and silver nanoparticles are, however, presented in Chapter 6 together with the case study results from the appended papers.

The included studies are discussed and categorized based on a number of aspects that are relevant from a risk perspective:

- Stressors assessed
- Fate modeling approaches
- Endpoints considered
- Risk indicators applied
- Geographical system boundaries

Table 2 presents all the included studies and the results of the categorization. Each aspect is discussed below in one section each.

#### **3.1 Stressors assessed**

Choosing which stressor to assess is a vital part of a risk assessment. As mentioned in Section 3.2, nanomaterials can be characterized according to different typologies based on their chemical composition or physical shape. Some risk assessments of nanomaterials assess stressors based on the physical shape of the nanoparticles. In a study by Boxall et al. (2007), the risks of a number of nanoparticulate materials were estimated: Silver, aluminum oxide, gold, cerium oxide, fullerenes, hydroxyapatite, latex, organo-silica, silicon dioxide, titanium dioxide, and zinc oxide. In the study by Johnson et al. (2011), the risk of titanium dioxide nanoparticles in sunscreen was estimated, and in the study by Praetorius et al. (2012), the risk due to exposure to titanium dioxide nanoparticles was estimated.

However, other risk assessments of nanomaterials do not clearly define the nanomaterial stressor according to the typology based on physical shape suggested by Foss Hansen et al. (2007). In the study by Gottschalk et al. (2009), the physical shapes of stressors such as carbon nanotubes and fullerenes are relatively well described. Although fullerenes can consist of varying numbers of carbon atoms, and carbon nanotubes can be both single- and multi-walled, these terms give a relatively clear description of both the chemistry and the shape of the stressor. Others are less clearly referred to as “nano titanium dioxide”, “nano zinc oxide” and “nano silver”. Gottschalk et al. (2011) use the same terms. The physical shape of the stressors assessed in these studies was thus not always clear. Other studies use the term nanoparticle interchangeably with less precise terms. In the study by Musee (2011), the risk of nanomaterials from cosmetics was assessed. In most of the study, the terms “nano titanium dioxide”, “nano silver” and “nano cerium dioxide” are used, but he refers to these stressors as nanoparticles in the abstract. Similarly, in the abstract of the study by O’Brien and Cummins (2010), the stressors are referred to as nanoparticles, but in the rest of the study the less precise terms “nano titanium dioxide” (released from exterior paint), “nano silver” (released from food packaging) and “nano cerium dioxide” (released from diesel fuel) are used. In the study by Blaser et al. (2008), they refer to silver nanoparticles several times, but the actual assessment is performed on antibacterial silver in plastics and textiles regardless of the physiochemical form of the silver.

The study by Quik et al. (2011) is different in that it does not aim at conducting a full risk assessment for specific nanomaterials, but rather at discussing a method for assessing exposure to nanoparticles in water. Thus, no specific stressors are considered in that study, but it is clear that the model is designed for nanoparticles and not for other types of nanomaterials.

Although the physical shape of the stressors is not stated in some of these studies, the chemical composition is always clearly stated. It is worth noting that the studies include a wide range of stressors with regards to chemical composition, although titanium dioxide and silver are studied more often than the others. Considering that silver is the most frequently found nanomaterial in consumer products, and titanium the third most frequently found (Project on Emerging Nanotechnologies 2012), this is not surprising.

### **3.2 Fate modeling approaches**

Considering that a number of review studies have discussed the fate of nanomaterials in the environment (Christian et al. 2008; Handy et al. 2008; Ju-Nam and Lead 2008; Klaine et al. 2008), it is interesting to review how fate modeling has been conducted in actual exposure and risk assessments of nanomaterials. In the study by Boxall et al. (2007), nanoparticle emissions from a number of sources were estimated, and distributed evenly in the environmental compartment to which they were emitted. No transport of nanoparticles between the compartments was included in the study. This method is similar to that applied in

the study by Musee (2011) and O'Brien and Cummins (2010). These methods can be described with this schematic equation:

$$\frac{dc}{dt} = \frac{\dot{m}_e}{V} \quad (7)$$

where  $c$  is the mass concentration of nanomaterials in a certain environmental compartment,  $t$  is the time,  $\dot{m}_e$  is the mass-based emissions of nanomaterials to the compartment from the socio-technical system, and  $V$  is the volume of the compartment. The term  $dc/dt$  corresponds to a time-resolved PEC. As can be seen in Eq. 7, no fate mechanisms for the nanoparticles are included. In these studies,  $\dot{m}_e$  is often operationalized as a constant annual emission of nanomaterials, and the time span considered is one year.

In contrast to the studies by Boxall et al. (2007) and Musee (2011), the study by Gottschalk et al. (2009), which is a further development of the early model by Mueller and Nowack (2008), allows for transfer of nanomaterials between different compartments. The model can thus be described with the following schematic equation:

$$\frac{dc}{dt} = \frac{f\dot{m}_{in}}{V} \quad (8)$$

where  $\dot{m}_{in}$  is the inflow of nanomaterials to the compartment from the socio-technical system (emissions) and from other environmental compartments, and  $f$  is a dimensionless partitioning factor that indicates which fraction of the emissions of nanomaterials to a compartment remains in the compartment. Here, fate mechanisms such as sedimentation are included, but they are not modeled mechanistically but aggregated into the partitioning factor. Eq. 7 can be seen as a special case of Eq. 8 with the partitioning factor equal to one. Note also that the partitioning factor can contain a number of different terms, quantifying the transport to different compartments.

The study by Gottschalk et al. (2011) focuses on the aquatic environment (in particular Swiss rivers), but the model is also based on Eq. 8. Emissions of nanomaterials to the river water are distributed across the country proportional to population density, assuming complete mixing of sewage water and river water. Two scenarios were applied for the transport of nanomaterials in rivers: one denoted  $S_0$  with complete nanomaterial removal between two river catchments, and one denoted  $S_c$  with no removal at all between two river catchments. It was suggested that these scenarios cover all possible fate scenarios for the nanomaterials and thus account for different values of the partitioning factor in Eq. 8 for different river sections. Thus, in the study by Gottschalk et al. (2011), the partitioning factor is  $f = [S_0, S_c]$ .

A number of studies attempt more mechanistic modeling approaches, but do not include nanomaterial-specific mechanisms. Blaser et al. (2008) conducted their risk assessment based on a river fate model and included sedimentation and diffusion between different layers of the

river in their model. These mechanisms were, however, generic for all physiochemical forms of silver. In the study by Johnson et al. (2011), fate modeling was conducted using the LF2000-WQX model, which is a model used for studying release of chemical substances from consumer products. This model has previously been used for organic contaminants in studies like that of Williams et al. (2009). The model combines hydrology and water quality models. The fate mechanisms included are thus the same as those for chemicals in the LF2000-WQX model, which include sorption, biodegradation, and volatilization. The relevance of this model to modeling the fate of nanomaterials is, however, unclear and is not extensively dealt with by Johnson et al. (2011).

The model equation by Quik et al. (2011) was developed based on the method of calculating exposure to chemical substances for aquatic organisms, but with the aim of developing nanomaterial-specific exposure models. It includes three fate mechanisms as indicated by the model equation:

$$\frac{dc}{dt} = \frac{\dot{m}_{in}}{V} - (k_{adv} + k_{sed} + k_{diss}) \times c \quad (9)$$

where  $k_{adv}$  is the rate constant for advection,  $k_{sed}$  is the rate constant of sedimentation and  $k_{diss}$  is the rate constant of dissolution. The rate constants all have units of the reciprocal of time. Advection occurs when nanoparticles are transported away by a stream of water. Sedimentation occurs when nanoparticles leave the water body and enter the sediment. In this paper, Quik et al. (2011) acknowledge that heteroagglomeration between nanoparticles and natural colloids plays an important role in the sedimentation of nanoparticles because the nanoparticles agglomerate with larger natural colloids, which sediment faster. The fate mechanism of heteroagglomeration is thus implicitly included in the sedimentation process. Dissolution means that the nanoparticles dissolve into ions or molecules. Some nanoparticles, such as silver and zinc oxide, dissolve relatively fast, whereas titanium dioxide nanoparticles hardly undergo any dissolution at all in natural waters. Quik et al. (2011) provides ranges of values for the rate constants ( $k_{adv}$ ,  $k_{sed}$ ,  $k_{diss}$ ) for specific nanoparticles in their study. These ranges are typically about two or three orders of magnitude, and no attempt to calculate the rate constants for a general case was done in the study.

In the study by Praetorius et al. (2012), exposure of nanoparticles in water was also assessed by trying to develop a mechanistic model analogous to those used for chemical substances. This resulted in a model that includes fate mechanisms such as heteroagglomeration, sedimentation, advection with the flow of the water body, bed load transport within the sediment, burial in the sediment, and resuspension from the sediment into the water. Some of these mechanisms, in particular heteroagglomeration, can indeed be regarded as nanomaterial-specific in the sense that they do not occur with ordinary chemicals.

From this review of fate modeling approaches, it seems that three different approaches can be distinguished: (1) modeling nanomaterial fate using aggregated partitioning factors, (2) applying mechanistic models without nanomaterial-specific fate mechanisms and (3) applying

nanomaterial-specific fate mechanisms. Of the reviewed studies, only the studies by Quik et al. (2011) and Praetorius et al. (2012) attempt to explicitly include nanomaterial-specific fate mechanisms in a similar manner to Paper I. For more detail see Section 5.2.

### **3.3 Endpoints considered**

The choice of ecological endpoints in risk assessment is important yet difficult (Suter 1989). In the existing risk assessments of nanomaterials, a large number of different endpoints are considered, indicating that it is currently unclear which endpoints are most threatened by specific nanomaterials. There is, however, a slight tilt towards aquatic organisms. Boxall et al. (2007) considered algae, fish, invertebrates, and bacteria. The assessment by Gottschalk et al. (2009) was performed for twelve different endpoints from different environmental compartments. Exactly the same endpoints were considered by Gottschalk et al. (2011). Blaser et al. (2008) considered three different water fleas living in water and sediment. The assessment by Johnson et al. (2011) was performed for the endpoints bacteria and earthworms. The assessment by Musee (2011) was performed for seven different aquatic organisms and one soil organism. In the assessment by O'Brien and Cummins (2010), a number of aquatic organisms were considered along with guideline values for drinking water for humans. Since only the exposure assessment step was considered by Quik et al. (2011) and Praetorius et al. (2012), no endpoints were discussed in those studies.

### **3.4 Risk indicator applied**

When assessing the risks of chemicals, a ratio between two mass concentrations (PEC/PNEC, Eq. 4) is normally used as risk indicator (Suter 1993a; van Leeuwen and Vermeire 2007). There have been extensive discussions on which risk indicator to use for nanomaterials, as reviewed in Paper I and Dhawan et al. (2009). Mass concentration is used in most of the reviewed risk assessments of nanomaterials (Boxall et al. 2007; Blaser et al. 2008; Gottschalk et al. 2009; O'Brien and Cummins 2010; Gottschalk et al. 2011; Johnson et al. 2011; Musee 2011; Quik et al. 2011). However, some of these studies discuss the possibility of other risk indicators. Musee (2011) suggested that surface area concentration, or variants thereof, may provide an alternative or additional risk indicator. O'Brien and Cummins (2010) discuss surface area concentration and particle number concentration as potential alternatives, and even carry out a simplified recalculation of their results into these indicators in order to investigate whether the relative exposure of the included nanomaterials would change considerably. The recalculation was based on the assumption of monodisperse particles. There is also a brief discussion of surface area concentration and particle number concentration as potential alternative exposure indicators in the report by Boxall et al. (2007). The study by Praetorius et al. (2012) is unique since it reports results both in terms of mass concentration and in terms of particle number concentration. A more thorough discussion of risk indicators for nanomaterials can be found in Section 7.3, in which the pros and cons of

mass concentration, particle number concentration, and surface area concentration are discussed.

### **3.5 Geographical system boundaries**

As mentioned in Section 2.2, risk assessments of chemicals can be conducted on different scales and consequently at different geographical resolutions. The reviewed risk assessments of nanomaterials have quite different geographical resolutions. Some were conducted on a national or continental scale. The assessment by Boxall et al. (2007) was conducted for the United Kingdom, and the assessment by Gottschalk et al. (2009) was conducted for Switzerland, the United States, and Europe. Some were conducted for specific rivers. The assessment by Gottschalk et al. (2011) was conducted for twenty-one river sections in Switzerland, the assessments by Blaser et al. (2008) and Praetorius et al. (2012) were conducted for the Rhine River in Europe and the assessment by Johnson et al. (2011) was conducted for the River Thames in the United Kingdom. The assessment by Musee (2011) was conducted for a specific city, Johannesburg in South Africa. The study by Quik et al. (2011) was conducted at a generic level and is not limited to a specific geographical location.

### **3.6 Lessons from the reviewed studies**

Lessons from the reviewed studies have influenced this thesis and the appended papers. First, the stressors considered in some early risk assessments informed the choice of which nanomaterials to study in the appended papers. Second, since nanomaterials are not only characterized by their chemical composition but also by their shape, it seemed relevant to be explicit about the physical shape of the stressor studied in risk assessments of nanomaterials. Attempts have therefore been made to avoid the imprecise description of the stressors that was found in some of the reviewed studies. Third, considering the differences between nanomaterials and chemicals with regard to environmental fate outlined by a number of authors and in Paper I, it seemed relevant to try to develop fate models specific to nanomaterials to ensure a relevant assessment instead of using the same models used for chemicals, as was done in some of the reviewed studies, particularly Johnson et al. (2011). This meant either developing nanomaterial-specific fate models or using partitioning factors that are applicable to nanomaterials. These two approaches have been explored in the appended papers. Fourth, considering the strong dominance of mass concentration as a risk indicator in the reviewed studies despite the discussion of other possible risk indicators for nanomaterials, the issue of the choice of risk indicator is frequently discussed in the appended papers. In some of the appended papers, particle number concentration was used instead of mass concentration.

Finally, it is interesting to note the considerable differences between the studies with regards to methods used and results obtained. For example, Boxall et al. (2007) estimated that the

concentrations of nanomaterials in soil would generally be orders of magnitude higher than the concentrations in water, but Musee (2011) estimated slightly higher concentrations in water. Considering the differences in geographical system boundaries and partitioning factor values, this in itself is not unexpected. However, it underlines the importance of further methodological discussion, and also the immaturity of the field of risk assessment of nanomaterials. The differences in the reviewed studies are so profound that the definition of risk based on comparing levels of toxic effects to exposure levels (Eq. 4) and the source-fate-endpoint model (Figure 3) seem to be the only thing these different methods have in common.

**Table 2.** Review of five exposure models for nanoparticles in aquatic environments. Abbreviations: Titanium dioxide (TiO<sub>2</sub>), aluminum oxide (Al<sub>2</sub>O<sub>3</sub>), gold (Au), cerium dioxide (CeO<sub>2</sub>), silica/silicon dioxide (SiO<sub>2</sub>), silver (Ag), zinc oxide (ZnO), and carbon nanotubes (CNT). Mass and particle number are short for mass concentration and particle number concentration, respectively.

Study	Fate modeling approaches	Stressors assessed	Endpoints considered	Risk indicator	Geographical boundary
Blaser et al. (2008)	Mechanistic, not nanomaterial-specific	Silver	3 water fleas	Mass	Rhine River
Boxall et al. (2007)	Partitioning factors	Nanoparticles from Ag, Al <sub>2</sub> O <sub>3</sub> , Au, CeO <sub>2</sub> , fullerenes, hydroxyapatite, latex, organo-SiO <sub>2</sub> , SiO <sub>2</sub> , TiO <sub>2</sub> , ZnO	Algae Fish Invertebrates Bacteria	Mass	United Kingdom
Gottschalk et al. (2009)	Partitioning factors	nano TiO <sub>2</sub> , nano ZnO, nano Ag, CNT, fullerenes	12 different	Mass	Switzerland United States Europe
Gottschalk et al. (2011)	Partitioning factors	nano TiO <sub>2</sub> , nano ZnO, nano Ag	12 different	Mass	Switzerland
Johnson et al. (2011)	Mechanistic, not nanomaterial-specific	TiO <sub>2</sub> nanoparticles	Bacteria Earthworms	Mass	River Thames
Musee (2011)	Partitioning factors	Ag and TiO <sub>2</sub> nanoparticles or nano Ag and nano TiO <sub>2</sub>	8 different	Mass	South Africa
O'Brien and Cummins (2010)	Partitioning factors	Ag, CeO <sub>2</sub> , and TiO <sub>2</sub> nanoparticles or nano Ag, nano CeO <sub>2</sub> , nanoTiO <sub>2</sub>	Aquatic organisms Humans	Mass	Ireland
Praetorius et al. (2012)	Mechanistic, nanomaterial-specific	TiO <sub>2</sub> nanoparticles	None	Mass Particle number	Rhine River
Quik et al. (2011)	Mechanistic, nanomaterial-specific	Nanoparticles in general	None	Mass	None



## 4 METHODS OUTLINED

The main aim of this thesis is to develop methods to contribute to the development of exposure assessment methods, and thus risk assessment methods, for nanomaterials. In Papers II and III, the method of particle flow analysis was developed from substance flow analysis. This method is described in Section 5.1. It can be used to assess emissions of nanoparticles, thus constituting the emission assessment part. Paper I outlined an exposure model based on colloidal stability theory. This model is described in Section 5.2. In this model, emissions are assumed but not calculated, and can therefore be said to include the whole exposure assessment, although the main focus is on the fate modeling part. In Paper IV, a method for assessing exposure of nanomaterials based on classical exposure modeling of chemicals was applied to the case of silver in clothes. This model includes the whole exposure and risk assessment, and is described in Section 5.3.

### 4.1 Prospective particle flow analysis

Authors have suggested using a substance life cycle approach for assessing emissions of nanomaterials (Sweet and Strohm 2006; Lubick 2008). As stated in Section 2.3, the industrial ecology method called substance flow analysis is commonly used to estimate emissions of substances of concern. Consequently, substance flow analysis became the point of departure for the development of emission assessment methods. However, in traditional substance flow analysis, mass is used as the indicator of magnitude, as in risk assessment of chemicals and material flow analysis. Inspired by the discussion of risk indicators for nanomaterials outlined in Paper I, Dhawan et al. (2009), and Section 4.5, particle number was used as an indicator of magnitude instead of mass in the emission assessments in some of the appended papers. This was done by modifying the substance flow analysis method into particle flow analysis. Although the particle flow analysis method is limited to using the particle number as an indicator of magnitude, it illustrates flexibility in the substance flow analysis method and its potential to be adapted to indicators of magnitude other than mass. Figure 8 presents a graphical illustration of the particle flow analysis model. In addition to changing the indicator of magnitude, this modification required a change in the substance flow analysis method. As noted above, in traditional substance flow analysis, the stock of a substance is calculated as:

$$\frac{dm}{dt} = \sum \dot{m}_{in} - \sum \dot{m}_{out} \quad (6)$$

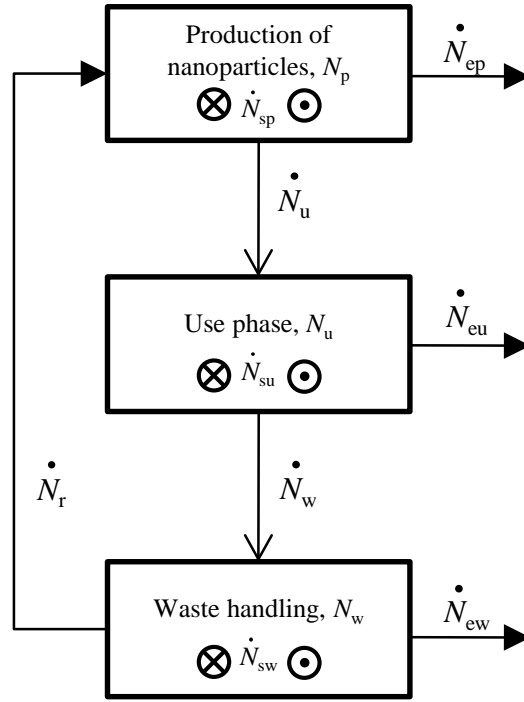
where  $\dot{m}$  represents mass flow and  $m$  represents the mass stock. This equation is basically the same as the law of mass conservation. However, although the mass of nanoparticles is conserved, the particle number may not be. Processes such as agglomeration, dissolution, melting, grinding, and weathering may increase or decrease the number of particles. This has

been included in the equation in the form of a sink/source term ( $\dot{N}_s$ ). The change in particle stock of a nanoparticulate material is calculated as:

$$\frac{dN}{dt} = \sum \dot{N}_{in} - \sum \dot{N}_{out} + \dot{N}_s \quad (10)$$

where  $N$  represents particle number stock,  $\dot{N}$  represents particle number flows, and the index  $s$  stands for source or sink. The parameter  $\dot{N}_s$  can be a source or a sink depending on its sign (positive or negative), that is, a sink is seen as a negative source. It is thus analogous to the loss functions used in fate modeling of chemicals, such as biodegradation (van de Meent and Bruijn 2007). As can be seen in Figure 8, for a certain product there can be source/sink terms in the production phase ( $\dot{N}_{sp}$ ), use phase ( $\dot{N}_{su}$ ) and waste handling phase ( $\dot{N}_{sw}$ ). In general,  $\dot{N}_{sp}$  is likely to be positive since the nanoparticles are being created from non-nanoparticulate materials. The particle number thus goes from basically zero to a larger number. It is more difficult to tell with  $\dot{N}_{su}$ . It is possible that agglomeration takes place in the use phase, thus reducing the particle number. It is also possible that weathering of particles creates more, smaller particles. The number could also remain largely unchanged. The  $\dot{N}_{sw}$  term is likely to be negative since many waste handling processes include high temperatures that could melt particles. Note, however, that this may differ for specific nanoparticles and products.

As it turned out, however, for the cases in Papers II and III, no sinks and sources of nanoparticles were identified except for the production of nanoparticles from non-nanoparticulate materials,  $\dot{N}_{sp}$ . However, this term was not treated explicitly but set equal to  $\dot{N}_u$ , as low emissions  $\dot{N}_{ep}$  were assumed during production as well as low recycling or reuse  $\dot{N}_r$  during waste handling.



**Figure 8.** Particle flow analysis model applied to quantify the flows and stocks of nanoparticles and the emissions of nanoparticles to the environment in Papers II and III.  $N$  denotes particle number stock,  $\dot{N}$  particle number flow, p production, u use phase, w waste handling, e emission, r recycling, and s denotes source. Note that  $\dot{N}_s$  may be negative, indicating a sink for particles (such as agglomeration) rather than a source (such as grinding). The symbols normally used for electronic current symbolize sinks and sources. Figure obtained from Papers II and III.

Besides using particle number as an indicator of magnitude, the particle flow analyses in Papers II and III have another feature that makes them different from previous studies. In previous studies, annual emissions of nanoparticles were approximated using annual production (Boxall et al. 2007; Blaser et al. 2008; Gottschalk et al. 2009; O'Brien and Cummins 2010; Gottschalk et al. 2011; Johnson et al. 2011; Musee 2011; Praetorius et al. 2012). This approximation is reasonable for cases where the annual emissions from the use phase are much larger than the waste flows. For these cases, the use phase stock is negligible, that is,  $\dot{N}_{eu} \gg \dot{N}_w$ ,  $N_u \approx 0$ , and  $\dot{N}_{eu} \approx \dot{N}_u$  in Figure 8. However, for cases where there is indeed a significant stock being built up in society, as with cement and electronics, annual emissions from the use phase may be very different from annual production. For those cases, emissions must instead be estimated as a function of the surface area of the stock or similar metric. Attempts to do so can be found in Papers II and III, for instance using the following equation:

$$\dot{N}_{eu} = A_u \times n_u \times k \quad (11)$$

where  $A_u$  is the surface area of the use phase product stock,  $n_u$  is the nanoparticle concentration in the product stock, and  $k$  is an emission factor with the unit m/s. Unfortunately, one difficulty with this method compared to approximating annual emissions by annual production is that it is difficult to obtain information about or estimate both the surface area of the stock  $A_u$  and the emission factor  $k$ . Eq. 11 should be seen as an attempt to produce an estimate. It may be that it needs to be simplified using fewer parameters, or made more complicated using additional parameters.

In addition to the development of particle flow analysis from substance flow analysis, a prospective approach was applied in the emission assessment, as suggested by other authors (Sweet and Strohm 2006; Wiesner et al. 2009). As described in Section 2.4, technologies at an early phase of development may enter the growth phase, undergo extensive diffusion, and eventually reach the mature, saturated phase in which the production and use of these technologies are higher. One way to apply a prospective approach to assessing future potential emissions is to not only consider the current state of technologies that make use of nanomaterials, but also a potential future state representing the mature phase. Although the current use of most products containing nanomaterials, and consequently nanomaterial emissions related to these products, may be low or non-existent, future emissions may be considerable when these technologies reach the mature phase of the technological life cycle. Considering only the use and emissions of the embryonic phase may thus give misleading results that may be falsely interpreted to imply that emissions of nanomaterials from an emerging technology will continue to be low in the future.

It is not obvious how to estimate this potential increase in use and subsequent emissions of nanomaterials. Although technology forecasts are sometimes made, there are many examples of forecasts which in hindsight have been misleading. An example is the forecast in the 1960s and 1970s that nuclear power would become the dominant source of energy at the turn of the century. This must be regarded as incorrect as nuclear power currently constitutes less than 10 percent of the global energy supply (Sandén 2004). However, relevant information may be obtained without applying forecasting methods. Explorative scenarios, which are future states or developments that are interesting to consider, offer an alternative (Börjeson et al. 2006). In contrast to forecasts, no statements are made regarding the probability of the explorative scenarios – they may be likely or unlikely, but should at least be possible. A similar concept called stylized states was applied by Hillman and Sandén (2008). These states represent possible future states that are interesting to consider in some respect. In Papers II and III, the explorative scenario considered was a world in which:

- The technology utilizing the nanomaterial has become the dominant design in its market.
- Everybody in the world uses as much of the technology per capita as high-income countries such as Sweden.
- The world population has increased to 10 billion people.

This explorative scenario constitutes a high-emission scenario. If even this scenario does not give rise to a considerable emission of nanoparticles, the technology will probably not cause high emissions in future. Applying explorative scenarios has provided valuable insights in Papers II and III. It has been shown that some technologies which are currently in a very early stage of technological development, such as self-cleaning cement containing titanium dioxide nanoparticles and clothing containing silver nanoparticles, have the potential to become much larger in the future. Thus they will give rise to considerably higher emissions than they currently do. Although this in itself is not unexpected, such insights will remain hidden if only the current production and use of nanomaterials are considered.

## 4.2 Exposure modeling of nanoparticles based on colloidal stability

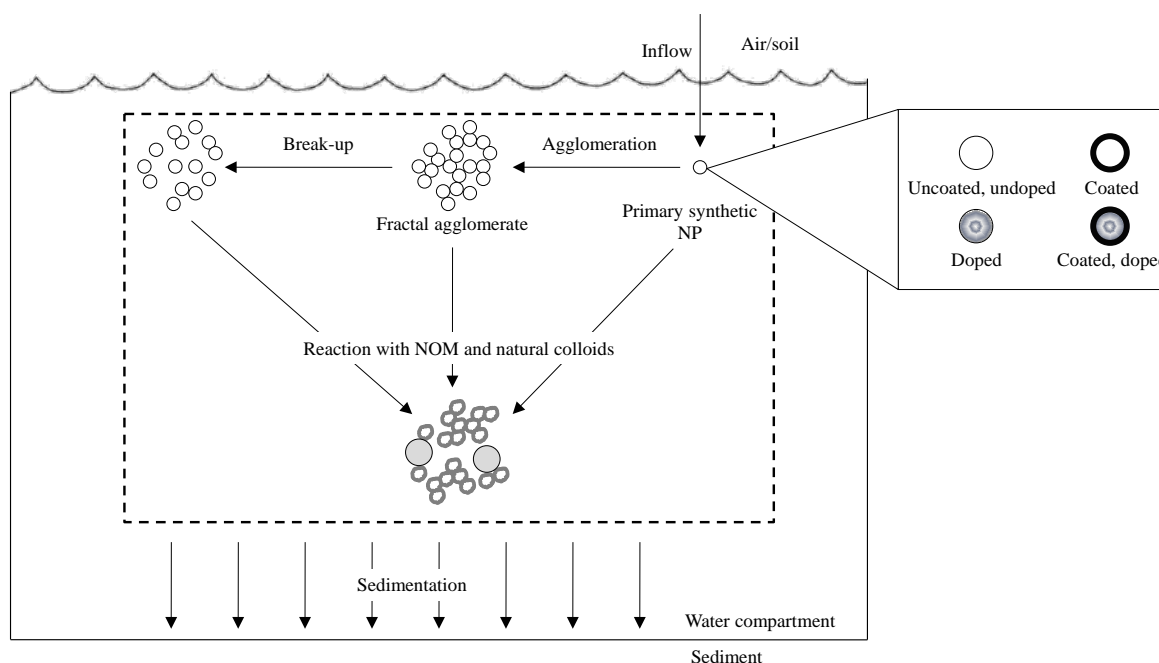
In Paper I, a bottom-up approach to exposure modeling of nanoparticles in water was attempted. Acknowledging that risk assessment of nanoparticles requires new methods and approaches, the literature on fate mechanisms was first reviewed. The result of that review can be seen in Figure 9. A number of fate mechanisms were identified:

- Homoagglomeration between nanoparticles of the same type.
- Sedimentation.
- Break-up between agglomerated particles.
- Reactions between nanoparticles and natural organic matter.
- Heteroagglomeration between nanoparticles and natural colloids.

In addition to these fate mechanisms, the fate of nanoparticles may also be altered by coating and doping of the particles (Figure 9). It was observed that studies that already tried to model some of these processes existed within the field of colloid chemistry. Colloids can be defined as dispersed particles within the size range of 1–1000 nm (Shaw 1992; Elimelech et al. 1995), thereby covering most of the size ranges that define nanomaterials (Section 3.1). Most notable was the early work by Smoluchowski (1917) and Friedlander (1977), which was further refined by Grant et al. (2001). These modeling attempts were based on colloidal stability theory and thus focused on homoagglomeration and sedimentation of colloidal particles. The main equation was extended in Paper I. A term describing a continuous inflow of particles was added, along with a term that could account for heteroagglomeration between synthetic nanoparticles emitted to the environment and natural colloids. The resulting equation became:

$$\frac{dn_j}{dt} = \frac{\dot{N}_{e,j}}{V} + \frac{1}{2} \sum_{i=1}^{i=j-1} \alpha_{i,j-i} K_{i,j-i} n_i n_{j-i} - n_j \sum_{i=1}^{i=\infty} \alpha_{i,j} K_{i,j} n_i - \frac{v_s}{d} j^\beta n_j - n_j \sum_{i=1}^{i=\infty} \alpha_{nc,i,j} K_{nc,i,j} n_{nc,i} \quad (12)$$

The term on the left side of the equation,  $dn_j/dt$ , describes the changes in concentration of an agglomerate with  $j$  primary particles. A summation of these terms over  $j$  and integration over a time span  $[0, t]$  corresponds to the particle number-based PEC of nanoparticles. The first term on the right side on the equation describes the emissions of an agglomerate with  $j$  primary particles to the water compartment. The second term describes the formation of agglomerates with  $j$  primary particles through agglomeration of particles  $i$  and  $j-i$ . The third term describes the loss of agglomerates with  $j$  primary particles through agglomeration with other particles  $i$ . The fourth term accounts for the sedimentation of agglomerates with  $j$  primary particles. The fifth term describes heteroagglomeration between agglomerates with  $j$  primary nanoparticles and natural colloids. This equation is based on the assumptions that all particles are approximately spherical and that merging of two particles is an irreversible reaction.  $n_j$  is the particle number concentration of agglomerates with  $j$  primary particles (i.e., if  $j$  equals three, then the agglomerate consists of three primary particles that have agglomerated),  $\alpha_{i,j}$  and  $\alpha_{i,j-i}$  are homoagglomeration collision efficiencies,  $K_{i,j}$  and  $K_{i,j-i}$  are rate constants,  $v_s$  is the sedimentation rate of primary particles,  $\beta$  describes the increase in sedimentation rate due to increased cluster size ( $2/3$  for spherical particles),  $d$  is the depth of the water compartment, and  $\dot{N}_{e,j}(t)$  is the particle-based emission of particle  $j$ ,  $\alpha_{nc}$  is the heteroagglomeration collision efficiency between nanoparticles and natural colloids,  $K_{nc}$  is the rate constant for collisions between natural colloids and synthetic nanoparticles, and  $n_{nc,i}$  is the particle number concentration of an agglomerate with  $i$  primary natural colloids. See Paper I regarding the units of the parameters in Eq. 12.



**Figure 9.** Illustration of fate mechanisms for nanoparticles in water, obtained from Paper I.

Compared to previous exposure and risk assessment models for nanoparticles and nanomaterials (Section 4.2), the model described in Eq. 12 goes further in trying to mechanistically explain nanoparticle fate from the perspective of colloid chemistry. It is also flexible in the sense that terms accounting for additional fate processes can be added to the equation. As shown by Arvidsson (2010), it is also possible to link this model to the particle flow analysis model. However, comparing Eq. 12 to Figure 9 shows that a number of important fate processes are not yet incorporated in the model. As was described in Paper I, the role of natural organic matter remains a puzzle. It can be indirectly included by modifying the collision efficiency  $\alpha$ , which is a factor between 0 and 1 that describes what fraction of collisions lead to a merging of the particles. Natural organic matter can alter the collision efficiency either by increasing the electrostatic repulsion or by providing steric hindrance or attraction. How this takes place is, however, not yet sufficiently understood to be quantified in an exposure model. Additional aspects not included in the model equation are doping and coating. Although a number of authors have highlighted the potential importance of these modifications (see Paper I), there currently is little knowledge of how these aspects affect the environmental fate of nanoparticles.

Another problem related to Eq. 12 is how to implement it in computer software. In Paper I, this was done in MATLAB. It turned out that the calculations were very time-consuming. Although improvements have been made to the program since the writing of Paper I, the general problem of computational power remains an issue to be considered when developing fate and exposure models for nanomaterials. Considering these difficulties, simplifications of Eq. 12 are warranted. As described in Section 4.2, Quik et al. (2011) proposed one such simplification. They argued that although agglomeration is a process that follows second order kinetics, as described in Paper I, it is possible that the majority of the particle collisions involving synthetic nanoparticles in the environment take place between a synthetic nanoparticle and a natural colloid, as natural colloids are much more numerous. Since the concentration of natural colloids is so much higher, it can be regarded as almost constant. Then the agglomeration will depend only on the concentration of synthetic nanoparticles in a pseudo-first order kinetic way. Indeed, complex kinetic fate processes are often modeled as pseudo-first order reactions for chemical substances in risk assessment of chemicals (Mill 1993). This situation would be much easier to model than Eq. 12. If it is further assumed that nanoparticles that agglomerate with natural colloids will sediment rather fast, that is, that heteroagglomeration is the bottleneck removal process, Eq. 12 can be simplified into:

$$\frac{dn_j}{dt} = \frac{\dot{N}_{e,j}}{V} - n_j \sum_{i=1}^{i=\infty} \alpha_{nc,i,j} K_{nc,i,j} n_{nc,i} \quad (13)$$

An approach similar to Eq. 13 was applied by Praetorius et al. (2012), although they included the sedimentation of nanoparticle-colloid agglomerates and pure nanoparticle agglomerates explicitly as in Eq. 12. Praetorius et al. (2012) also modeled size classes rather than individual particles, that is, the index  $j$  in their study did not represent individual agglomerates but five different size classes of agglomerates (16, 212, 408, 604, and 800 nm in diameter). Having

$j = [1,5] \in \mathbb{N}$  rather than  $j = [1, >1000] \in \mathbb{N}$  as in Paper I constitutes a simplification that greatly reduces the need for computational power. Even further simplifications can be made if it is assumed that all particles entering the water compartment are of the same primary particle size and that the natural colloids are similar enough to be characterized by one single particle size:

$$\frac{dn}{dt} = \frac{\dot{N}_e}{V} - n\alpha_{nc}K_{nc}n_{nc} \quad (14)$$

Additional motivation for treating homoagglomeration as negligible was provided by Quik et al. (2012). They showed that in water from the two European rivers the Rhine and the Meuse, first order heteroagglomeration was the main mechanism for sedimentation of cerium dioxide nanoparticles. Based on this, an equation similar to Eq. 14 was suggested for exposure modeling of nanoparticles in natural water. However, for filtered water with very few natural colloids, second order homoagglomeration was shown to be the main mechanism for sedimentation. This raises the question of application domain for Eq. 13 and Eq. 14. Do they work well for all natural waters, or are there natural waters with a low content of natural colloids, such as Alpine streams, for which they are not applicable? If it can be further shown that Eq. 13 or Eq. 14 are applicable to most natural waters, their simplicity compared to Eq. 12 makes them attractive for future exposure modeling of nanoparticles in water. If not, it may be necessary to start from the more complex Eq. 12 or similar approaches that include homoagglomeration.

Unfortunately, the models presented in Paper I and by Praetorius et al. (2012) share a common problem, namely that they both require collision efficiencies ( $\alpha$  and  $\alpha_{nc}$ ) as input data. As mentioned above, collision efficiencies can be affected by the presence of natural organic matter in complex ways that are difficult to predict. In addition, collision efficiencies are difficult to calculate and measure even without the presence of natural organic matter. Existing models, which are based on the so-called DLVO theory (Derjaguin and Landau 1941; Verwey and Overbeek 1948), have been deemed to offer little guidance (Wiesner 1992). The difficulty of obtaining values for collision efficiencies constitutes a problem for mechanistic exposure modeling of nanoparticles that must be overcome if these methods are to be extensively used. A recent study successfully modeled collision efficiency by considering whether the kinetic energy of the nanoparticles is high enough to overcome interaction energy barriers (Zhang et al. 2012). This method may provide a fruitful way forward, although the approach may be limited to smaller nanoparticles.

### 4.3 Exposure modeling using partitioning factors

In Paper IV, a method was outlined for the specific purpose of assessing the risks posed by antibacterial silver in clothes used in urban areas. The specific area studied in Paper IV was Gothenburg, Sweden. The risks considered were those to wastewater treatment sludge and



agricultural land. Note that this method is considered to apply to both silver nanoparticles and other forms of silver. It is not known exactly which forms of silver are used in antibacterial clothing, although there are indications that silver in the form of nanoparticles may be the most attractive form of silver from a technical point of view (Nowack et al. 2011). Fortunately, it seems that ionic and nanoparticulate silver emitted from clothing will exhibit similar emission rates and fate within the scope of Paper IV. There was thus no reason to differentiate between different forms of silver in Paper IV. In Paper IV, the emissions of silver were estimated as:

$$\dot{m}_e = PAc_{\text{clothes}}f_{\text{em}} \quad (15)$$

where  $P$  is the population using the wastewater treatment plant,  $A$  is the per capita consumption of silver clothing,  $c_{\text{clothes}}$  is the mass concentration of silver in the clothes, and  $f_{\text{em}}$  is the dimensionless fraction of silver emitted. This equation is similar to the industrial ecology method called the IPAT equation, which in its simplest form can be written:

$$I = PAT \quad (16)$$

where  $I$  stands for (environmental) impacts,  $P$  for population,  $A$  for affluence and  $T$  for technology, implying that these last three factors are those that affect the environmental impacts. An early version of this equation was developed by Ehrlich and Holdren (1971) and later modified by Commoner et al. (1971) and others (Chertow 2000). In Eq. 15, the environmental impact is emissions of silver, the consumption of silver clothing corresponds to affluence, and  $c_{\text{clothes}}$  and  $f_{\text{em}}$  are parameters describing characteristics of the technology of silver clothing.

Following the emission assessment, the fate of the emitted silver through wastewater treatment was investigated. It was found that most silver would probably end up in the wastewater treatment sludge. The sludge could then be used as fertilizer on agricultural land. Thus, the fate of the silver in soil was modeled. This resulted in an exposure model to assess the exposure of silver, for instance in the form of nanoparticles, from antibacterial clothing to organisms in soil:

$$\frac{dc_{\text{soil}}}{dt} = \frac{\dot{m}_e f_{\text{sludge}} \dot{m}_{\text{soil}}}{V_{\text{soil}} \dot{m}_{\text{WWTP}}} \quad (17)$$

where  $c_{\text{soil}}$  is the concentration of silver in the soil,  $\dot{m}_{\text{WWTP}}$  is the amount of sludge produced in the wastewater treatment plant each year,  $\dot{m}_{\text{soil}}$  is the amount of sludge applied to the soil each year,  $V_{\text{soil}}$  is the volume of the soil compartment,  $f_{\text{sludge}}$  is the dimensionless fraction of the silver entering the wastewater treatment plant which ends up in the sludge, and  $M$  is the annual mass of dry sludge produced.

This linear equation is similar to traditional exposure models for chemicals in soil, such as Eq. 4.32 in van Leeuwen and Vermeire (2007) for calculating the concentration of chemicals in soil, although fate mechanisms such as evaporation, degradation, and leaching have been excluded in Eq. 17 for reasons explained in Paper IV.

It should be noted that this model is more aggregated than the exposure modeling based on colloidal stability performed in Paper I and described in Section 5.2. Rather than addressing agglomeration and sedimentation in detail, these fate mechanisms are included in the model by the partitioning factor  $f_{\text{sludge}}$ . This partitioning factor indicates what fraction of the silver ends up in the sludge ( $f_{\text{sludge}}$ ) (i.e., which portion of the silver will sediment), and which portion will remain in the water ( $1-f_{\text{sludge}}$ ). It became apparent that ionic silver is likely to exhibit the same partitioning factors as silver nanoparticles in this case. Thus the partitioning factors are the same for both nanoparticulate and ionic silver in this case.

Eq. 17 is analogous to the general Eq. 7 and thus similar to other approaches in previous risk assessment studies of nanomaterials described in Section 4.2. An example is the approach with the scenarios  $S_0$  and  $S_c$  applied by Gottschalk et al. (2011): the complex processes of agglomeration and sedimentation are modeled by a partitioning factor which indicates the fraction of the nanomaterials that remain in the water and how much sediments out. Eq. 17 is also similar to the models used to assess direct input of nanoparticles to soil by Boxall et al. (2007) and Musee (2011). It can, however, be argued that the use of partitioning factors in Paper IV is more extensively motivated based on mechanistic arguments than in previous risk assessment studies on nanomaterials. The partitioning factor in Paper IV is derived and used based on data from Swedish wastewater treatment plants and arguments from colloidal stability theory, whereas in other risk assessment studies on nanomaterials the partitioning factor approach is less rigorous.

## 5 CASE STUDY RESULTS

Although the main outcomes of this work are methods and reflections on methods, some results from the case studies are worth mentioning. These are presented below for each of the three cases studied, namely titanium dioxide nanoparticles, silver nanoparticles, and graphene.

### 5.1 Titanium dioxide nanoparticles

Titanium dioxide nanoparticles are perhaps the most studied stressors within the field of nanomaterial risk assessment. The potential risks associated with their use in sunscreen were among the first to be noted by groups such as the environmental non-governmental organization Friends of the Earth (2006, 2007). Some authors argued that the titanium dioxide nanoparticles would probably not be taken up via the human skin during sunscreen use, and that the risks to humans from this use of titanium dioxide nanoparticles would therefore be low (e.g., Nohynek et al. (2007)). However, since sunscreen is sometimes applied before swimming, aquatic organisms may potentially be exposed to the nanoparticles. This hypothesis was strengthened by the early risk assessment study by Mueller and Nowack (2008), which showed that nano-titanium dioxide posed the highest risk to aquatic organisms of all the nanomaterials and endpoints included in that study. Subsequent risk assessment studies have not confirmed this result. Johnson et al. (2011) concluded that titanium dioxide nanoparticles from sunscreen probably did not pose a risk to aquatic organisms in the River Thames. Boxall et al. (2007) showed no risk of titanium dioxide nanoparticles in the United Kingdom. Although the results of Gottschalk et al. (2009) showed a risk from nano-titanium dioxide in sewage treatment plant effluent, the risk was higher for both nano-silver and nano-zinc oxide. Gottschalk et al. (2011) showed risk for nano-titanium dioxide in Swiss rivers, but only in urban and industrial areas. Musee (2011) showed risk for nano-titanium dioxide in aquatic environments in Johannesburg, but only for the maximum emission and low dilution scenario.

In the appended papers, the risk of titanium dioxide nanoparticles was not studied in itself. The results of Paper I did however reveal that the value of the collision efficiency ( $\alpha$ ) and the emissions of titanium dioxide nanoparticles to the water compartment have a considerable impact on the PEC of titanium dioxide nanoparticles. If the collision efficiency was high, the particle number-based PEC in the water was low due to heavy agglomeration and sedimentation. If the collision efficiency was low, the particle number-based PEC in the water became considerably higher. As expected, higher emissions also resulted in a higher PEC. Changes in other parameters in the model did not result in any changes in the PEC within the range in which they were varied.

In Paper II, emission of titanium dioxide nanoparticles was studied using particle flow analysis. Three different products were investigated with regard to the particle number-based

use phase consumption, use phase stocks, and use phase emissions. These were sunscreen, paint, and self-cleaning cement. In sunscreen, the titanium dioxide nanoparticles are used as a UV light blocker and absorbent. In paint, they are used as the white pigment. In self-cleaning cement, they are used for their photocatalytic properties (and partly also as white pigment). Estimates of the current annual global use phase consumption results are similar for sunscreen and paint. This is noteworthy, since in terms of mass, the consumption of titanium nanoparticles in paint is much larger due to the much larger volumes of paint produced annually. But the particles in sunscreen are much smaller on average, so on a particle number basis, the use of titanium dioxide nanoparticles in sunscreen is much higher. In comparison, the current use of titanium dioxide nanoparticles in self-cleaning cement is negligible. The only significant use phase stock is that of titanium dioxide nanoparticles in paint. As for current emissions, the importance of sunscreen in spite of its comparatively low mass-based annual production becomes even clearer. Only a fraction of the titanium dioxide nanoparticles in paint are emitted from the surface of the societal stock, whereas most sunscreen consumed each year is emitted to the environment in the use phase. Sunscreen is thus the dominant source for emissions of titanium dioxide nanoparticles (Figure 10).

Applying the explorative scenario method outlined in Section 5.1 changes this picture somewhat, and results in titanium dioxide nanoparticles in cement becoming the by far largest annual global use phase consumption and stock. This is largely due to the high annual production of cement and the small size of the nanoparticles used in that product. However, when looking at emissions, sunscreen is still the dominant contributor (Figure 10). This is again due to the dissipative nature of the use of sunscreen, causing direct emissions to the environment rather than slow release from the surface of a stock. Still, since not even the worst-case scenario by Johnson et al. (2011) showed any risk of titanium dioxide nanoparticles from sunscreen to organisms living in the River Thames, it is unclear whether these potentially high emissions of titanium dioxide nanoparticles from sunscreen are reason for concern. This does, however, raise the question of whether there still would be no risk if the mass-based risk assessment by Johnson et al. (2011) had been conducted on a particle number basis instead. It could be that although the mass-based emissions of titanium dioxide nanoparticles from sunscreen are small even at high consumption rates of sunscreen, the particle number-based emissions are high enough to cause adverse effects. Unfortunately, there are currently no toxicological studies in which particle number-based toxicity thresholds are reported for titanium dioxide nanoparticles, so such assessments are not yet possible. Considering the clear tendency of titanium dioxide nanoparticles to agglomerate in natural waters, recalculating mass into particle number under the assumption of monodisperse particles would be questionable, as will be shown in Section 7.3.



**Figure 10.** Current and future potential global emissions of titanium dioxide nanoparticles in paint, sunscreen and self-cleaning cement. The potential future emissions are estimated based on an explorative scenario. For self-cleaning cement, current emissions are negligible. Based on results from Paper II.

## 5.2 Silver nanoparticles

Since silver is the most frequently used nanomaterial in consumer products (Project on Emerging Nanotechnologies 2012) and has previously been of environmental concern when used for photographic purposes (Luoma 2008), it comes as little surprise that silver nanomaterials are one of the most frequently studied nanomaterials from a risk perspective. However, the results from risk assessment studies are somewhat varied. Studies by Blaser et al. (2008), O'Brien and Cummins (2010), Musee (2011), and Boxall et al. (2007) did not identify any risk posed by nano-silver and silver nanoparticles. Gottschalk et al. (2009) showed that nano-silver constitutes a risk in surface water and, to a larger extent, in sewage treatment plant effluent. Gottschalk et al. (2011) showed risk for nano-silver in Swiss rivers in urban and industrial areas. In addition, arguments that are not based on risk assessments have been made regarding the environmental risks of nano-silver and silver nanoparticles. Nowack (2010) argue that nano-silver would probably bind to sulphide during wastewater treatment, which would considerably reduce its toxicity. Although this has been reported by other authors as well (e.g., Blaser et al. (2008)), and is partly accounted for in Paper IV, this argument in itself is not sufficient to assess the risks of silver nanoparticles. It could be that future emissions will become high enough to cause adverse effects despite the lower toxicity of sulphide-bound silver nanoparticles. Nowack et al. (2011) argue that colloidal silver (similar to silver nanomaterials) has been used for a long time and that silver nanomaterials should therefore not be considered a new phenomenon. However, the implications of this argument for the magnitude of the risks of silver nanoparticles are unclear. For example, the

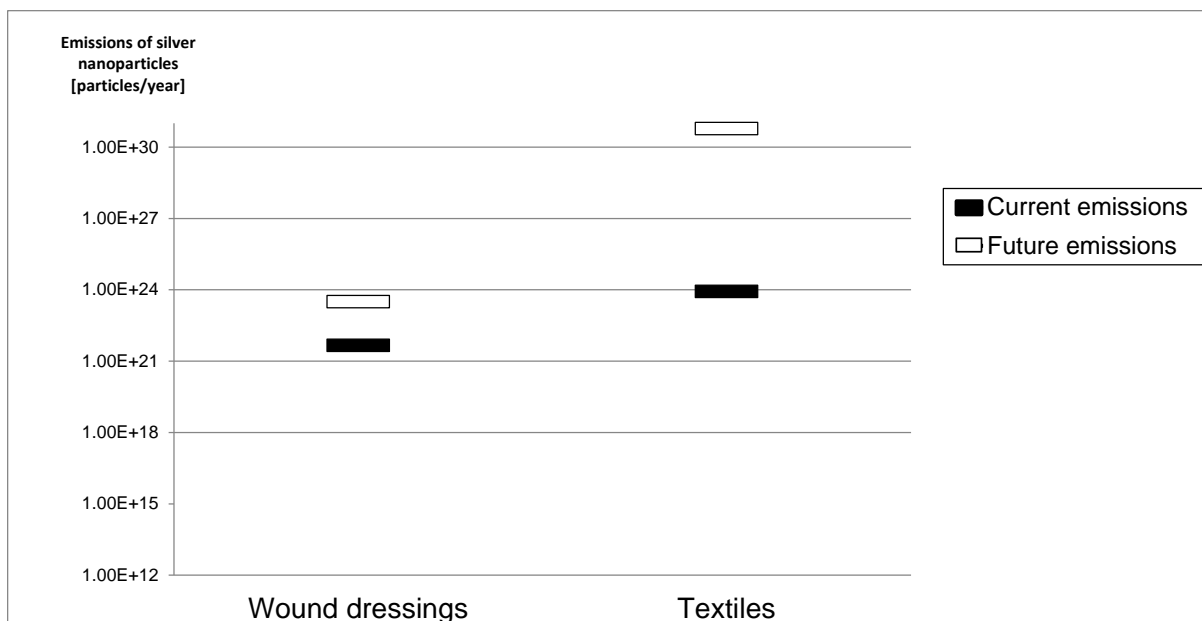
use of silver nanoparticles as an antibacterial agent and subsequent emissions may become much larger in future, so that environmental risks not previously present may emerge. There is also discussion regarding whether silver nanoparticles will persist in the environment or dissolve into silver ions. So far, the results are somewhat ambiguous (Elzey and Grassian 2010; Liu and Hurt 2010; Li and Lenhart 2012).

Paper III reports on a particle flow analysis study similar to the one conducted for titanium dioxide nanoparticles. The three products studied for silver nanoparticles were wound dressings, clothing, and electronic circuitry. In the first two, silver is used as antibacterial agent, whereas in the last, silver is used for its high conductivity. The current global consumption and emissions of silver nanoparticles related to these three products are largely unknown, and wound dressings are the only product for which it was possible to obtain an exact number (Figure 11). Electronic circuitry is the only product likely to form a significant societal stock, although the current magnitude of this stock is unknown, and consequently also the related emissions. For textiles, it was possible to obtain only upper boundaries of current consumption, stock, and emissions for reasons explained in Paper III (Figure 11). The future explorative scenario revealed that clothing was potentially the largest contributor to consumption and emissions of silver nanoparticles. Again, the considerable variation of silver content in clothing only makes it possible to obtain an estimated range, but even the lower-end consumption and emissions of that range are higher than those of wound dressings and electronic circuitry. The consumption of silver nanoparticles in wound dressings in the explorative scenario is also uncertain, but seems to be lower than that of electronic circuitry. It was not possible to obtain data on emissions of silver nanoparticles from electronic circuitry, and as a result no emissions from this technology could be calculated.

The study reported in Paper IV was conducted based largely on the results of Paper III, knowing that clothing containing antibacterial silver has the potential to give rise to high silver emissions. In Paper IV, the risks related to antibacterial silver ending up in sludge after being washed out of clothing were investigated. The study was conducted because the silver concentration in the sludge of the Rya wastewater treatment plant in Gothenburg had increased between 2007 and 2008. Such an increase had not been observed for decades, and raised the question of whether emerging use of antibacterial silver could be the reason for the increase. The study in Paper IV is not restricted to silver nanoparticles, but the approach is valid for other forms of silver as well. This approach was chosen since there is little or no information on which forms of silver are present in a given antibacterial fabric. But there seem to be no major differences in the fate of different forms of silver during wastewater treatment – nanoparticulate and other forms of silver will all probably primarily end up in the sludge. Clothing as a source of the silver was selected for two reasons: (1) Paper III suggested that clothing is the most prominent consumer product source of antibacterial silver, and (2) it was possible to derive emission factors from published data. The estimated concentrations of silver in sludge were benchmarked against risk-related threshold values for silver in sludge. The estimated concentrations of silver in soil were compared to different toxicity thresholds for earthworms, including both toxicity of silver nanoparticles and non-nanomaterial silver sulphide.

The results of Paper IV first and foremost indicate the importance of the magnitude of the emissions of silver, which depends on the silver content in clothing. The measured values of the silver content in clothing varied by six orders of magnitude. The highest values resulted in very high emissions and consequently high concentrations of silver in the sludge – enough to exceed all risk-related guideline values applied in the study, even with modest consumption of silver-containing clothing. However, for the lowest value of silver content, even very high consumption of silver clothing did not result in any risk exceeding any of the risk-related guidelines. The same applied when assessing the risk to earthworms from applying the silver-containing sludge to soil as fertilizer. For high silver concentrations in clothing, various toxicity thresholds would likely be exceeded even with modest consumption of silver-containing clothing. But for low silver concentration in clothing, even high consumption would not result in any risk to earthworms. The main recommendation from the study was therefore to keep the silver content of antibacterial clothing low in order to avoid environmentally adverse effects. Two relevant stakeholders were identified, namely the companies producing antibacterial clothing and the regulatory authorities. Companies can limit the silver content of clothing by design choices, and authorities can regulate the maximum allowable silver content in clothing.

The work conducted on silver in Papers III and IV suggests that the differences in the environmental fate and toxicity of silver nanoparticles compared to ionic silver may not be the greatest reason for concern. The discussions on whether silver nanoparticles are more toxic than ionic silver and whether silver nanoparticles will remain or dissolve into ions in the environment are ongoing and ambiguous. The benefit of applying silver nanoparticles to consumer products from a technical point of view compared to other techniques for silver application is clearer and less questioned (Nowack et al. 2011). The greatest reason for concern with regard to silver nanoparticles may thus not be their high toxicity or different environmental fate, but rather their potential to increase the use of antibacterial silver in consumer products and thus cause larger emissions.



**Figure 11.** Current and potential future emissions of silver nanoparticles from wound dressings and textiles. The potential future emissions are estimated based on an explorative scenario. The current emission results for textiles are based on upper boundaries of production rate, and both the current and future emission results for textiles are based on upper boundaries for silver content in clothing. Based on results from Paper III.

### 5.3 The nanomaterial graphene

Graphene was the most challenging of the nanomaterials studied in this work. There is currently very little risk-related data for this nanomaterial. Only some estimates of annual production exist, and only a few toxicity studies have been conducted (see Paper V). However, based on a review of existing data, a number of reasons for concern were highlighted in Paper V:

- Graphene has the potential to be produced in large amounts.
- Graphene seems to be chemically persistent and hydrophobic.
- Graphene has significant toxicity according to toxicity studies.

These reasons for concern are not enough to assess the risks of graphene. As described above, a risk assessment requires quantification of both exposure and effects. Available data only reveal that in the future organisms may have considerable exposure to graphene in light of the potentially high production rate, its persistence, and its hydrophobicity. The data also suggest that the toxicity of graphene is considerable, at least to the endpoints (human cells and bacteria) investigated in the studies reviewed in Paper V. Although it is currently too early to tell whether graphene does pose risks to human health and the environment, it can be concluded that graphene is a hazard (see Section 2.1), but that the magnitude of the risk cannot yet be estimated.



Although Paper V cannot be used to prove that graphene constitutes a risk, the results are interesting from the point of view of reflexive innovation systems. Graphene is in the early stages of commercialization, with estimated production rates of 15 metric tonnes in 2009 and 200 metric tonnes in 2010 or 2011 (Segal 2009). A number of new applications for graphene are being developed, for example, within energy production and storage (Brownson et al. 2011) and composite materials (Li and Zhong 2011). Now would be the time to conduct assessments of the environmental risks of graphene in order to ensure safe use of this technically marvelous material in the future and prevent it from becoming yet another chemical late lesson, joining the group already populated by PCB, halocarbons, and asbestos.

Concern is even more justified in light of the answers given by a number of researchers interviewed for Paper V. Some of them responded defensively when questioned about the risks of graphene and argued that graphene does not constitute a risk. This view was usually based on arguments that must be considered weak from a risk assessment point of view, such as the similarities between graphene and graphite. Graphene has unique properties different from those of graphite, as shown in Paper V. If graphene were so similar to the well-known graphite, one might wonder why researchers working with graphene were awarded the Nobel Prize in physics in 2010. The conviction among these scientists that graphene is safe may discourage risk-related studies on graphene and thus not facilitate reflexive innovation in this area of materials science.

## 6 REFLECTIONS ON RISKS OF NANOMATERIALS

This work has resulted in a number of different outcomes. Some of them are methods that can be used and further developed by other researchers (see Chapter 5). Others are case study results concerning specific nanomaterials (see Chapter 6). But there are also more indirect outcomes, such as reflections on the definition of nanomaterials and on which indicator to use when assessing the risks of nanomaterials. This chapter is about those less definite but still important outcomes.

### 6.1 Focus on hazardous properties rather than definitions

The idea of defining nanomaterials can be expressed mathematically as the search for a way to categorize a general stressor  $S$  according to the set {nano, not nano}. The search is thus for a function  $f: S \rightarrow \{\text{nano, not nano}\}$ . The most common approach to perform this categorization is to use length  $x$  of the different dimensions of the stressor, such as the diameter of particles, and investigate whether this length is within a certain range:

$$f(x) = \begin{cases} \text{if } a \leq x \leq b: S = \{\text{nano}\} \\ \text{if } x > b \text{ or } x < a: S = \{\text{not nano}\} \end{cases} \quad (18)$$

As mentioned in Section 3.1, the lower boundary  $a$  can be 0.1 nm, 1 nm, or undefined. The most usual lower boundary is probably 1 nm. The upper boundary  $b$  can be 500 nm or, more commonly, 100 nm. This diversity in size range indicates that the values of  $a$  and  $b$  are, if not arbitrary, at least not self-evident. Strong reasons are seldom given for the chosen size range. In fact, it is often stated that the size range is “approximately” 1–100 nm (British Standards Institution 2007; ISO 2008), “roughly” 1–100 nm (Foss Hansen et al. 2007) or “typically” 1–100 nm (Sweet and Strohm 2006). Perhaps the most dubious suggestion is the definition with no lower boundary  $a$  at all, only an upper boundary  $b$ , since that would mean that chemical stressors such as PCB and mercury are considered as nanomaterials (British Standards Institution 2007).

It is clear that defining nanomaterials according to a size range is problematic. From a narrow risk assessment point of view, the choice of size range definition has implications. Consider a hypothetical case: a lake with a content of 10 mg/l of the stressor  $S$ . Assume that the PNEC of the nano-form of  $S$  is 1 mg/l based on conducted ecotoxicological studies. Further assume that 1 percent of  $S$  is particles of size 1–100 nm, and the other 99 percent is particles of size 100–500 nm. Also assume that the PNEC of bulk  $S$  is much higher, say 1000 mg/l. In this case, assuming that 1 nm is the lower boundary, risk or no risk is determined by whether the upper boundary of the nanomaterial size range is set to 100 nm or 500 nm:

$$RQ_{1-100 \text{ nm}} = \frac{PEC}{PNEC} = \frac{0.1}{1} = 0.1 < 1$$

$$RQ_{1-500 \text{ nm}} = \frac{PEC}{PNEC} = \frac{10}{1} = 10 > 1$$

The recent definition suggested by the European Commission (2011) states that 50 percent of the particle number size distribution should be in the size range of 1–100 nm in order for  $S = \{\text{nano}\}$ . This definition introduces a secondary indicator besides the length  $x$ : The fraction of the particle distribution that lies within the size range, here denoted  $r$  for ratio. The function then becomes:

$$f(x, r) = \begin{cases} \text{if } a \leq x \leq b \text{ and } r > q: S = \{\text{nano}\} \\ \text{if } a \leq x \leq b \text{ and } r < q: S = \{\text{not nano}\} \\ \text{if } x > b \text{ or } x < a: S = \{\text{not nano}\} \end{cases} \quad (19)$$

As mentioned in Section 2.1, the European Commission suggests that the boundary for  $r$ , here denoted  $q$ , should be 50 percent. However, as with the size range boundaries  $a$  and  $b$ , the reasons for the choice of this number are not extensively motivated and seems arbitrary. It could also be said that the definition suggested by the European Commission seems to cover only particles and does not include nano-structured surfaces. This makes it different from most other suggested definitions.

The definition mentioned in the study by Foss Hansen et al. (2007), stating that a nanomaterial, in addition to being of a certain size, must have additional properties different from those of the bulk form of the stressor, has caused some puzzlement. Adding this to the definition is meant to differentiate between older nanomaterials, such as metal colloids used for dyeing glass in churches (Erhardt 2003), and newer nanomaterials. Mathematically, it further divides the possible states of the stressor  $S$  into the set  $\{\text{new nano, old nano, not nano}\}$ , of which only the state  $\{\text{new nano}\}$  is assumed to be of interest in terms of risk assessment of nanomaterials. However, this definition contains two problematic words, namely *property* and *bulk form*. Which properties are to be regarded? If particle size is a property, then any nanoparticle should be counted as a nanomaterial, and then this additional requirement does not add much to the definition based on size range. And what is meant by bulk form? Chemical substances may have several bulk forms. For instance, graphene consists of polyaromatic monolayers of carbon, which together form the bulk material graphite. But diamond is a bulk material that also consists only of carbon, but in another crystalline form. Titanium dioxide has three bulk forms: anatase, rutile, and brookite. These bulk forms all have different properties, sometimes very different (see Paper V). Does a nanomaterial need to have properties different to one of its bulk forms, or all of them? This novelty definition seems to be at least as problematic to apply as the size range definition. There seems to be no general indicator that can be used when it comes to categorizing  $S$  into the set

{new nano, old nano, not nano}. The categorization seems to be based on subjective views of what is new and what is old. There may also be mismatches between the novelty and size range definitions, since new material properties may not always be exhibited within the 1–100 nm size range (British Standards Institution 2007).

To complicate the issue of nanomaterial definition further, it was noted in several of the appended papers that whether a stressor  $S$  is nano or not nano can vary in time. A stressor can cease to be a nanomaterial, for instance when silver nanoparticles dissolve into silver ions. A non-nanomaterial stressor can also become a nanomaterial, as when nano-sized titanium dioxide films are created through vapor deposition of titanium chloride. When studying stressors from an environmental systems analysis perspective, for instance in terms of their substance life cycles and environmental fate, their categorization according to the {nano, not nano} set may thus fluctuate.

Considering these varying views and the problems related to the definition of nanomaterials, it is perhaps not surprising that nanomaterials have been defined somewhat differently in the appended papers. In Papers I–III, a size range definition of 1–500 nm was applied. This was justified by the importance from a risk perspective of making conservative assessments of the risk, and thus choosing the highest known suggested value of the upper boundary  $b$ . In Paper IV, the studied stressor is silver in general, including nano-sized silver. Since the model is assumed to be applicable to all kinds of silver, including all possible nano-forms, no specific definition of nanomaterials was needed in that study. In Paper V it is noted that graphene fits all known definitions of nanomaterials except for the definition by the European Commission that only seems to count particles as nanomaterials.

It is valuable from a risk assessment perspective to have some knowledge about the stressor studied. However, science-based categorization of stressors according to the {nano, not nano} set seems to be futile for the general case. This was also suggested by Maynard (2011), who stated that “a sensible definition has proved hard, if not impossible, to arrive at”. This does not mean that particles with a diameter between 1–100 nm cannot be labeled as nanoparticles. But it does suggest that more effort should be put into investigating in which physiochemical forms certain stressors constitute risk, and less effort into investigating whether the stressors should be labeled as nanomaterials. Consider, for example, chromium, which is very toxic to humans as a  $\text{Cr}^{6+}$  ion, but less so in other forms. Therefore, different guideline values exist for  $\text{Cr}^{6+}$  and for other forms of chromium (e.g., the Swedish Environmental Protection Agency (1997)). The stressor chromium is thus categorized according to the set  $\{\text{Cr}^{6+}, \text{other Cr}\}$  from a risk assessment perspective. Finding such sets based on differences in environmental fate and toxicity for stressors which may be nanomaterials seems to be more relevant from a risk assessment perspective than debating whether they actually are nanomaterials. To take another example, a review of ecotoxicity studies on nanoparticles revealed little difference in mass concentration-based toxicity between the nano and bulk forms of zinc oxide (Kahru and Dubourguier 2010). If the environmental fate of these two forms of zinc oxide were also similar, there would be little reason to differentiate between them from a risk assessment

perspective. An example of a categorization based on risk-related properties could perhaps be whether the stressor is rod-shaped or not, {rod, not rod}, as it appears that in general rod-shaped stressors such as asbestos (Harremoës et al. 2001) and carbon nanotubes (Poland et al. 2008) can cause more damage to lungs than can spherical stressors.

## 6.2 Data scarcity

Data scarcity is common within systems science (Miser and Quade 1985) and has been especially prominent in this work because of the novelty of nanomaterials. Exposure models for chemical substances are heavily dependent on input data, and the same is true for exposure models for nanomaterials. For many nanomaterials, such exposure-related data is not available. This problem is highlighted in all of the appended papers.

Possibly the most crucial exposure-related data that has been lacking are emission factors describing the rate at which nanomaterials are emitted from society to the environment. These factors can be formulated in different ways, the most simple of which is probably the fraction of the substance released within one year. Without such information, it is extremely difficult to assess the risks of nanomaterials. Lack of data on environmental fate can partly be compensated for by crude modeling approaches that do not require extensive data. Although crude, such an approach may provide a better assessment of the exposure than a mere guess. But emission factors are required to obtain even an order of magnitude estimation of emissions. This was a major problem in Paper V. Emissions of graphene from, for example, a composite material may be 1 percent per year, 0.01 percent per year, 0.0001 percent per year, or something completely different. There are no such measurements for graphene, few measurements of emission factors for nanomaterials in general, and no models to aid even order of magnitude estimates of emission factors. Studies from which emission factors may be derived exist only for a limited number of nanomaterials and uses, such as silver nanomaterials in consumer products (Benn and Westerhoff 2008; Geranio et al. 2009; Benn et al. 2010; Kaegi et al. 2010; Swedish Chemicals Agency 2011), titanium dioxide nanoparticles in paint (Kaegi et al. 2008), titanium dioxide nanopowder coatings (Hsu and Chein 2007), and carbon nanotubes from composites (Movahedi 2008). The existence of a number of such studies for silver in clothing made it possible to perform the calculations in Papers III and IV. If sound risk assessments of nanomaterials are to be conducted, more effort must be put into deriving emission factors for different nanomaterials in different products.

In addition, data on the use of products containing nanomaterials is often lacking, and when available, it is often reported in terms of money rather than physical flows. For example, consumption of clothing is typically reported in terms of money spent rather than mass bought. In theory, data on production and consumption can be obtained from consumers and companies via surveys or interviews. The problem is that such studies are time-consuming, and there is no guarantee that companies would answer. Contacts with producers of antibacterial silver and products containing antibacterial silver during the work presented in

Papers III and IV did not result in any data. Another study also stated that companies are unwilling to answer questions about their production volumes of nanomaterials (Hendren et al. 2011). Thus, despite putting time and money into such surveys and interviews, there is no guarantee that companies will be willing to share information. Consumers may be more eager to answer such surveys, but may not always know whether they are consuming products that contain nanomaterials due to lack of information on consumer products.

Much more could be written about data scarcity, and many examples from the appended papers could be repeated. It is clear that if risk assessment is to keep up with innovation in nanomaterials, additional mechanisms that provide risk-relevant data are required.

### **6.3 Risk indicators for nanomaterials**

Three different risk indicators have been suggested for exposure to and effects of nanomaterials (see Paper I and Dhawan et al. (2009)). These are mass concentration, particle number concentration, and surface area concentration. In this section, the pros and cons of these indicators are discussed.

Mass concentration is used as an exposure and effect indicator in risk assessment of chemicals and in mass-flow models for chemical substances (van Leeuwen and Vermeire 2007; MacLeod et al. 2010). The law of conservation of mass makes mass-based calculations convenient. Much of the available basic data on nanomaterial production is reported in terms of mass, and recalculation into other indicators requires information that may not always be available. The vast majority of the toxicological and ecotoxicological studies on nanomaterials are conducted on a mass basis (Baun et al. 2008; Kahru and Dubourguier 2010), although a few were conducted on a surface area basis (Oberdörster et al. 2005; van Hoecke et al. 2008). It is therefore difficult to use results from exposure assessments with indicators other than mass for calculating risk quotients and performing a full risk assessment. If indicators other than mass concentration are to be used in risk assessment of nanomaterials, it requires effort from both exposure assessors and toxicologists. Considering the entrenched position of mass in risk assessment, production reporting, and toxicology, it is not surprising that the literature review presented in Section 4.4 shows that most risk assessment studies of nanomaterials use mass concentration as the risk indicator (Table 1).

Particle number has so far only been applied as a risk indicator in Papers I–III and in the study by Praetorius et al. (2012). However, particle number has two advantages over mass as a risk indicator for nanoparticles. The first advantage is that particles are more relevant, in the sense that what a fish swimming in a lake contaminated by nanoparticles actually encounters are discrete particles. This is similar to the case of chemicals, for which molecules or atoms rather than mass would be encountered by a swimming fish. But the number of molecules or atoms is proportional to the mass according to the following equation:

$$m = \frac{MN}{N_A} \quad (20)$$

where  $N$  is the number of molecules or atoms,  $m$  is the mass,  $M$  is the molar mass of the substance, and  $N_A$  is Avogadro's constant. The ratio  $N/N_A$  is referred to as the amount of a substance in chemistry. For nanoparticles, however, there is no similar way to relate mass and particle number. If it is assumed that the particles are monodisperse, that is, not agglomerated at all, the following expression may be used to convert between particle number and mass:

$$m = \frac{\rho\pi d^3}{6N} \quad (21)$$

where  $N$  stands for particle number,  $m$  for mass,  $\rho$  for density, and  $d$  for particle diameter. However, considering that agglomeration of particles in the environment is likely (see for instance Paper I), this expression is probably inaccurate for most cases.

The second advantage of particle number is that it is compatible with agglomeration and sedimentation models such as the one described in Paper I and Section 5.2. The reason for this is that agglomeration takes place mechanistically by merging of discrete particles or agglomerates, creating larger agglomerates that will sediment at a faster rate. Sedimentation depends on the mass of the discrete object, whether particle or agglomerate. There is no way to tell whether a dispersion of 1 mg/l of particles will sediment without knowledge of the agglomeration behavior and the size and density of the particles or agglomerates. Mass alone cannot provide this information. However, a clear drawback of particle number as risk indicator is that it can only be applied to nanoparticles, and not to other nanomaterials.

There are no risk assessments of nanomaterials in which surface area is used as risk indicator, but there are some toxicity studies in which surface area is applied as an effect indicator (e.g., van Hoecke et al. (2008) and Oberdörster et al. (2005)). The reason for the interest in surface area in toxicology is that some toxic effects from nanomaterials are believed to arise mechanistically from interactions between the endpoint and the surface of the nanomaterial (Nel et al. 2006). Surface area may therefore be the most relevant risk indicator from an effect assessment point of view. Regarding exposure assessment, however, modeling the emissions and fate of nanomaterials in terms of surface area has not been attempted in this thesis. Nor is it known to have been attempted by other authors. The reason for this is probably the dynamic nature of surface area. For monodisperse nanoparticles the surface area  $A$  can be calculated from the mass  $m$  and density  $\rho$ :

$$A = 4\pi \left( \frac{3m}{4\pi\rho} \right)^{2/3} \quad (22)$$

However, for nanoparticles in the environment, this equation would not hold. The particles would agglomerate, sediment, and bind to natural colloids and natural organic matter. These processes would alter the surface area in ways that cannot yet be predicted by models. Although it may be relevant from a toxicological point of view, surface area concentration as risk indicator thus constitutes a major challenge for exposure assessment.

On the basis of the two advantages mentioned above, Papers I–III argue that particle number is a more appropriate risk indicator for nanoparticles. But in Paper IV, it was concluded that considering that silver nanomaterials may dissolve into silver ions, and that both will probably experience a similar fate during wastewater treatment and in soil, mass was sufficiently relevant for the calculations. The question of which risk indicator to use for nanomaterials is strongly linked to the question of the need for novel exposure assessment methods for nanomaterials, and to novel effects caused by nanomaterials. If exposure models based on mass appear to be sufficient, and if agglomeration and sedimentation can be described and modeled sufficiently well on a mass basis, the two main advantages of particle number fall away. The question of how to distinguish whether mechanistic agglomeration and sedimentation models are required for a relevant assessment of the risk of nanoparticles is discussed further in Section 7.5. A risk indicator for nanomaterials must also be relevant to both exposure and effect assessment. Finding a risk indicator that is relevant and feasible for both exposure and effect assessment constitutes a challenge that should be further engaged by risk assessors, chemists, and ecotoxicologists.

## **6.4 Proxy risk indicators**

Other approaches have been suggested as alternatives to risk assessment of chemicals. These approaches have different names, such as the precautionary approach (Santillo and Johnston 1999), proxy measures (Berg and Scheringer 1994), and the hazard-based approach (Löfstedt 2011). In this thesis, they are referred as proxy risk indicators. Proxy indicators are indicators that are correlated or linked to some attribute which is not directly observable (Gallopín 1996). The risk of chemicals is a good example of such an attribute. The use of proxy risk indicators for chemicals can be justified by the considerable complexity of the environment and organisms living in the environment (Berg and Scheringer 1994). Their use has been claimed to be more precautionary and scientific than risk quotients in light of the high uncertainty related to the models used to derive risk quotients (Santillo and Johnston 1999). Examples of proposed proxy risk indicators for chemicals include their persistence, emissions, spatial range (Scheringer and Berg 1994), and of course also their toxicity. Using similar arguments about the considerable complexity of the environment and its organisms, Azar et al. (1996) proposed that chemical sustainability could be assessed from annual emissions and degradation rates of synthetic chemicals, thus avoiding the need to model the complex environment.

In some studies, proxy risk indicators have been applied to assess the risks of nanomaterials. For example, Grieger et al. (2011) assessed risk in a proxy-fashion using the two indicators,



protected units (PUs) and causes of risk (CRs). PUs are populations of organisms of interest to be protected, such as algae in water. CRs are ways for the stressor to induce harm, such as forming reactive oxygen radicals and inducing cell swelling. The importance of these two indicators is ranked on a three-point scale {1, 2, 3} with 1 corresponding to low importance and 3 to high importance. If both the PU of algae in water and the CR of production of reactive oxygen are ranked as a 3, that is, if  $\{PU, CR\} = \{3, 3\}$ , the risk of oxygen radical formation in algae in water is considered high. Unlike the proxy risk indicators suggested by Scheringer and Berg (1994) and Azar et al. (1996), the PU and CR focus on toxic effects rather than potential exposure.

Data scarcity has been a major obstacle in the appended papers, and this makes less data-demanding proxy risk indicators attractive for assessment of the risks of nanomaterials. However, proxy risk indicators for nanomaterials, as well as for chemicals, face a problem when it comes to showing a strong connection between the proxy indicator and the risk. It can be argued that a low ranking of PU and CR is no guarantee of low risk, since emissions and consequently exposure may be very high for a particular nanomaterial. If only the toxicity of a nanomaterial is known, it is difficult to make a relevant assessment of its risks. The same is true for other proxy risk indicators such as persistence and emissions. Although proxy risk indicators are useful because of the immense complexity of the environment (Berg and Scheringer 1994) and because they reduce the need for risk-related data, there is also a possibility that important risk-related aspects may be left out of an analysis based on proxy risk indicators. The risk quotient (RQ, Eq. 4) is holistic in the sense that it incorporates data on emissions, persistence, long-range transport, toxicity, and other parameters into one single indicator. Still, considering the immense difficulties in deriving RQs for nanomaterials as pointed out in this thesis and elsewhere, proxy risk indicators for nanomaterials may constitute a relevant approach. Further discussion and studies of proxy risk indicators for nanomaterials would help to reveal the relevance of that approach.

## **6.5 A call for collaboration on exposure assessment of nanomaterials**

A number of chemists have advocated the need for a new risk assessment paradigm for nanomaterials, stating that assessing the risks of nanomaterials requires the inclusion of novel, nanomaterial-specific aspects (e.g., Klaine et al. (2008), Handy et al. (2008), Lubick (2008), Wiesner et al. (2009) and Owen and Handy (2007)). There are a large number of experimental chemistry studies on nanomaterials, in particular nanoparticles. The studies often describe the measurement of some physiochemical property of the nanoparticles, such as their zeta potential, collision efficiency and electrophoretic mobility. The introductions to these studies often claim that their research will aid in the assessment of risks related to nanoparticles. Often, the authors claim that an accurate assessment of the risks of nanoparticles must be based on detailed knowledge of their chemistry as “the devil is in the details” (Mudunkotuwa and Grassian 2011). Some criticism of the risk assessments conducted has been expressed by such chemists, for instance the comment of Wiesner et al. (2009) primarily on the work of

Gottschalk et al. (2009): “Such simple models are entirely appropriate for poorly characterized systems, but they offer limited guidance.”

Indeed, it can be argued that many of the risk assessment studies reviewed in Chapter 4 are crude and premature. However, although there is little doubt that some physiochemical data on nanomaterials is required in order to make a relevant risk assessment, the call for detailed, mechanistic risk models made by some chemists must be nuanced. The environment is too complex to ever be described in full detail for risk assessment purposes (Berg and Scheringer 1994). Risk assessment methods always require simplifications of reality – the question is which simplifications can be made without making the assessment irrelevant. Furthermore, exactly how the detailed experimental studies on nanomaterials performed by chemists relate to exposure and risk is not always made clear in their studies. Even a very detailed model with an output parameter such as electrophoretic mobility will not aid risk assessment unless the connection between this output parameter and exposure and risk is made clear.

As mentioned in the review conducted in Section 4.2, there are a number of different modeling approaches for exposure assessment of nanomaterials. Some apply mechanistic, nanomaterial-specific models, and others apply aggregated partitioning factors to model complex processes. It is too early to tell which of these methods is the most promising. In order to say something about which of these models are most relevant for further development, collaboration between risk assessors and chemists is required. Surely, chemists have ideas about which mechanisms are important to include in a model, and perhaps also about how to model them. It is also necessary to collaborate in order to ensure measured data for the models, and to ensure that risk assessors do not include parameters in their models for which the availability of measured data cannot be ensured. More collaboration between chemists and risk assessors could also prevent chemists from conducting studies on self-claimed risk-related properties of nanomaterials that have an unclear connection to exposure and risk. Instead, experimental studies could be conducted on nanomaterial properties that have an explicit role in risk models, for instance the collision efficiency. Collaboration may also ensure that risk models are designed to include the parameters that chemists consider important from a risk perspective. And perhaps most importantly, collaboration is necessary in order to be able to compare modeling results with experimental measurements in order to validate the models. Such collaborations are crucial for developing harmonized exposure assessment methods for nanomaterials.

## 7 CONCLUSIONS AND FUTURE RESEARCH

The aim of this work was to contribute to the development of risk assessment methods for nanomaterials, in particular the development of emission and exposure assessment methods. The contributions to the development of risk assessment methods for nanomaterials are mainly the methods outlined in this thesis:

- The method of prospective particle flow analysis for assessing emissions of nanoparticles developed in Papers II and III.
- Exposure modeling for nanoparticles based on colloidal stability outlined in Paper I.
- Exposure modeling using partitioning factors outlined in Paper IV.

The second aim was to apply the developed methods to assess the risks of selected nanomaterials. This has resulted in a number of case study results:

- Collision efficacy was shown to have a considerable impact on the agglomeration and sedimentation behavior of titanium dioxide nanoparticles in Paper I.
- Sunscreen is currently the largest source of titanium dioxide nanoparticle emissions, and may remain so in the future if the high-emission scenario in Paper II is realized.
- Textiles treated with silver nanoparticles for antibacterial purposes are currently the largest source of silver nanoparticles, and may remain so in the future according to the high-emission scenario in Paper III.
- Antibacterial silver in clothing, possibly in nanomaterial forms, can cause high concentrations in sludge and soil if the concentration of silver in clothing is not controlled, according to the assessment in Paper IV.
- Knowledge about the environmental and health risks of graphene is very limited according to the review in Paper V. The current data gives some reason for concern due to the potentially high production rate, hydrophobicity, and considerable toxicity of graphene.

In addition to methods and case study results, this work has resulted in some reflections on risk assessment of nanomaterials:

- It is currently difficult to determine the most relevant risk indicator for nanomaterials. Mass, particle number, and surface area concentrations constitute possible options, and all have different pros and cons.
- Existing definitions of nanomaterials are questionable from a risk assessment point of view, and more effort should be expended in investigating which types of stressors are extra hazardous, rather than trying to find a one-size-fits-all definition of nanomaterials.
- Data scarcity is currently profound and obstructs risk assessments of nanomaterials.

- Proxy risk indicators may constitute a relevant alternative approach to assessing the risks of nanomaterials.
- In order to obtain more risk-relevant data and develop exposure models for nanomaterials, more collaboration between risk assessors and chemists would be helpful, since chemists know best what can be measured and how, whereas risk assessors know best what would be interesting to measure from a risk perspective.

These contributions should be seen as a number of small steps towards a harmonized method for risk assessment of nanomaterials. A number of issues for future research, which would take the field even closer to this goal, have been identified in this thesis:

- Additional case studies using the methods outlined in this thesis, that is, prospective particle flow analysis, exposure modeling of nanoparticles based on colloidal stability, and exposure modeling of nanomaterials using partitioning factors, would help to develop these methods and reveal their strengths and limitations. In particular, the application domains of Eq. 13 and Eq. 14 should be investigated.
- The nanomaterials studied in this thesis have provided interesting cases. However, other nanomaterials should also be investigated. For example, a study by Aschberger et al. (2011) ranked zinc oxide as the most risky of five studied nanomaterials. Concerns have also been raised regarding the extensive exposure of many people to cerium dioxide nanoparticles used as fuel additive (Cassee et al. 2011).
- One way to determine the merits of developed risk models and indicators for nanomaterials is to compare the results from experimental measurements and risk models. Although none of these methods are flawless, mutual cross-validation may provide a way towards a harmonized risk assessment method for nanomaterials.
- The profound data scarcity in the field of risk assessment of nanomaterials must be remedied. Deriving emission coefficients and collecting data on production of nanomaterials constitute two important goals for future research. Regardless of which fate modeling approach is considered most relevant, data on emissions to the environment will always constitute important input to such models.
- Further studies on proxy risk indicators for nanomaterials would help to reveal the relevance of such an approach as an alternative to risk assessment.
- Further studies by risk assessors, chemists and ecotoxicologists on the relevance of different risk indicators for nanomaterials should be conducted.

Finally, all three nanomaterials studied in this thesis are what are known as passive nanomaterials (Roco 2004; Tour 2007). Active nanomaterials are currently not as developed, and risk-related data for them is probably even scarcer than for graphene. It is also possible that other definitions of risk than the one applied in this thesis, that is, the risk quotient in Eq. 4, are required to assess the potentially more complex risks related to active nanomaterials. Still, considering the possible shift towards active nanomaterials (Subramanian et al. 2010), they constitute an important topic for future research.

## 8 REFERENCES

Abbott, L. C. and A. D. Maynard (2010). Exposure assessment approaches for engineered nanomaterials. *Risk Analysis* 30(11): 1634-1644.

Abernathy, W. J. and J. M. Utterback (1978). Patterns of industrial innovation. *Technology Review* 80(7): 40-47.

Ackoff, R. L. (1973). Science in the systems age: Beyond IE, OR, and MS. *Operations Research* 21(3): 661-671.

Adams, J. (1995). *Risk*. Padstow: TJI Digital.

Adriaanse, A., S. Bringezu, A. Hammond, Y. Moriguchi, E. Rodenburg, D. G. Rogich and H. Schütz (1997). *Resource flows: The material basis of industrial economies*. Washington DC: World Resource Institute.

Allard, P., A. Fairbrother, B. K. Hope, R. N. Hull, M. S. Johnson, L. Kapustka, G. Mann, B. McDonald and B. E. Sample (2010). Recommendations for the development and application of wildlife toxicity reference values. *Integrated Environmental Assessment and Management* 6(1): 28-37.

Aristotle (350 BCE). *Nicomachean ethics. Book i, chapter 3*. Translated by W. D. Ross.

Arvidsson, R. (2010). *Towards perspective exposure modeling of nanoparticles - applying particle flow analysis and kinetic exposure modeling for the cases of TiO<sub>2</sub> and Ag nanoparticles*. Gothenburg: Chalmers University of Technology.

Aschberger, K., C. Micheletti, B. Sokull-Klüttgen and F. M. Christensen (2011). Analysis of currently available data for characterising the risk of engineered nanomaterials to the environment and human health — lessons learned from four case studies. *Environment International* 37(6): 1143-1156.

Ayres, R. U. and U. E. Simonis (1994). *Industrial metabolism: Restructuring for sustainable development*. New York: United Nations University Press.

Azar, C., J. Holmberg and K. Lindgren (1996). Socio-ecological indicators for sustainability. *Ecological Economics* 18(2): 89-112.

Baccini, P. and P. H. Brunner (1991). *Metabolism of the anthroposphere*. Berlin: Springer.

Baumann, H. and S. J. Cowell (1999). An evaluative framework for conceptual and analytical approaches used in environmental management. *Greener Management International* (26): 109-122.

Baumann, H. and A.-M. Tillman (2004). *The hitchhiker's guide to LCA: An orientation in life cycle assessment methodology and application*. Lund: Studentlitteratur.

- Baun, A., N. Hartmann, K. Grieger and K. Kusk (2008). Ecotoxicity of engineered nanoparticles to aquatic invertebrates: A brief review and recommendations for future toxicity testing. *Ecotoxicology* 17(5): 387-395.
- Beck, U. (1992a). From industrial society to the risk society: Questions of survival, social structure and ecological enlightenment. *Theory, Culture & Society* 9(1): 97-123.
- Beck, U. (1992b). *Risk society. Towards a new modernity*. London: SAGE Publications.
- Bedford, T. and R. Cooke (2001). *Probabilistic risk analysis - foundations and methods*. Cambridge: Cambridge University Press.
- Benn, T., B. Cavanagh, K. Hristovski, J. D. Posner and P. Westerhoff (2010). The release of nanosilver from consumer products used in the home. *Journal of Environmental Quality* 39(6): 1875-1882.
- Benn, T. M. and P. Westerhoff (2008). Nanoparticle silver released into water from commercially available sock fabrics. *Environmental Science & Technology* 42(18): 7025-7026.
- Berg, M. and M. Scheringer (1994). Problems in environmental risk assessment and the need for proxy measures. *Fresenius Environmental Bulletin* 3: 487-492.
- Blaser, S. A., M. Scheringer, M. MacLeod and K. Hungerbühler (2008). Estimation of cumulative aquatic exposure and risk due to silver: Contribution of nano-functionalized plastics and textiles. *Science of The Total Environment* 390(2-3): 396-409.
- Boholm, Å. and H. Corvellec (2010). A relational theory of risk. *Journal of Risk Research* 14(2): 175-190.
- Boxall, A. B. A., Q. Chaudhry, C. Sinclair, A. Jones, R. Aitken, B. Jefferson and C. Watts (2007). *Current and future predicted environmental exposure to engineered nanoparticles*. York: Central Science Laboratory.
- Brett, D. W. (2006). A discussion of silver as an antimicrobial agent: Alleviating the confusion. *Ostomy Wound Management* 52(1).
- Bringezu, S., M. Fischer-Kowalski, R. Kleijn and V. Palm (1998). Regional and national material flow accounting: From paradigm to practice of sustainability. ConAccount Workshop, Leiden, Wuppertal Special.
- Bringezu, S. and Y. Moriguchi (2002). Material flow analysis. *A handbook of industrial ecology*. R. U. Ayres and L. W. Ayres. Cheltenham: Edward Elgar.
- British Standards Institution (2007). *Terminology for nanomaterials*. London: PAS (Publicly Available Specification) 136:2007.
- Brownson, D. A. C., D. K. Kampouris and C. E. Banks (2011). An overview of graphene in energy production and storage applications. *Journal of Power Sources* 196(11): 4873-4885.

- Brunner, P. H. (2010). Substance flow analysis as a decision support tool for phosphorus management. *Journal of Industrial Ecology* 14(6): 870-873.
- Burgman, M. A. (2005). *Risks and decisions for conservation and environmental management*. Cambridge, UK: Cambridge University Press.
- Börjeson, L., M. Höjer, K.-H. Dreborg, T. Ekvall and G. Finnveden (2006). Scenario types and techniques: Towards a user's guide. *Futures* 38(7): 723-739.
- Cain, A., S. Disch, C. Twaroski, J. Reindl and C. R. Case (2007). Substance flow analysis of mercury intentionally used in products in the united states. *Journal of Industrial Ecology* 11(3): 61-75.
- Cairns, J. J. and D. S. Cherry (1983). A site-specific field and laboratory evaluation of fish and asiatic calm population responses to coal fired power plant discharges. *Water Science and Technology* 15: 31-58.
- Carson, R. (1962). *Silent spring*. Boston: Houghton Mifflin.
- Cassar, L., C. Pepe, G. Tognon, G. L. Guerrini and R. Amadelli (2003). White cement for architectural concrete, possessing photocatalytic properties. Proceedings of the 11th International Congress on the Chemistry of Cement, Skokie, IL, USA: Portland Cement Association.
- Cassee, F. R., E. C. van Balen, C. Singh, D. Green, H. Muijser, J. Weinstein and K. Dreher (2011). Exposure, health and ecological effects review of engineered nanoscale cerium and cerium oxide associated with its use as a fuel additive. *Critical Reviews in Toxicology* 41(3): 213-229.
- Checkland, P. (1993). *Systems thinking, systems practice*. Baffins Lane: John Wiley & Sons.
- Chertow, M. (2000). The IPAT equation and its variants. *Journal of Industrial Ecology* 4(4): 13-29.
- Christian, P., F. Von der Kammer, M. Baalousha and T. Hofmann (2008). Nanoparticles: Structure, properties, preparation and behaviour in environmental media. *Ecotoxicology* 17(5): 326-343.
- Colborn, T. and C. Clement (1992). *Chemically induced alterations in sexual and functional development: The wildlife/human connection*. Princeton: Princeton Scientific Publishing Co., Inc.
- Colborn, T., D. Dumanoski and J. P. Myers (1997). *Our stolen future*. New York: Penguin Books.
- Collingridge, D. (1980). *The social control of technology*. London: Frances Pinter.
- Colvin, V. L. (2003). The potential environmental impact of engineered nanomaterials. *Nature Biotechnology* 21(10): 1166-1170.

Commoner, B., M. Corr and P. J. Stampler (1971). *The closing circle: Nature, man, and technology*. New York: Knopf.

Côté, R. P. and P. G. Wells (1991). *Controlling chemical hazards. Fundamentals of the management of toxic chemicals*. London: Unwin Hyman Ltd.

Crichton, M. (2002). *Prey: A novel*. New York: HarperCollins.

Curran, M. A., P. Frankl, R. Heijungs, A. Köhler and I. S. Olsen (2007). *Nanotechnology and life cycle assessment - a systems approach to nanotechnology and the environment*. Washington DC: Woodrow Wilson International Center for Scholars - Project on Emerging Nanotechnologies.

David, P. A. (1985). Clio and the economics of QUERTY. *American Economic Review* 75(2): 332-337.

Davies, J. C. (2009). *Oversight of next generation nanotechnologies*. Washington DC: Woodrow Wilson International Center for Scholars, Project on Emerging Nanotechnologies and The PEW Charitable Trusts.

Derjaguin, B. and L. Landau (1941). Theory of the stability of strongly charged lyophobic sols and of the adhesion of strongly charged particles in solutions of electrolytes. *Acta Physicochimica URSS* 14: 633-662.

Dhawan, A., V. Sharma and D. Parmar (2009). Nanomaterials: A challenge for toxicologists. *Nanotoxicology* 3(1): 1-9.

Drexler, E. (1986). *Engines of creation: The coming era of nanotechnology*. New York: Anchor Book.

Dubois, A. and L.-E. Gadde (2002). Systematic combining: An abductive approach to case research. *Journal of Business Research* 55(7): 553-560.

Ehrlich, P. R. and J. P. Holdren (1971). Impact of population growth. *Science* 171(3977): 1212-1217.

Elimelech, M., J. Gregor, X. Jia and R. I. Williams (1995). *Particle deposition and aggregation: Measurement, modeling, and simulation*. Woburn: Butterworth-Heinemann.

Elzey, S. and V. Grassian (2010). Agglomeration, isolation and dissolution of commercially manufactured silver nanoparticles in aqueous environments. *Journal of Nanoparticle Research* 12(5): 1945-1958.

Erhardt, D. (2003). Materials conservation: Not-so-new technology. *Nature Materials* 2(8): 509-510.

Eriksson, E., H. R. Andersen and A. Ledin (2008). Substance flow analysis of parabens in denmark complemented with a survey of presence and frequency in various commodities. *Journal of Hazardous Materials* 156(1-3): 240-259.



European Chemicals Agency (2011). *Guidance on information requirements and chemical safety assessment, chapter R.2-R.20*. Helsinki.

European Commission (2011). *Commission recommendation of 18 october 2011 on the definition of nanomaterial*. Brussels.

Finnveden, G., M. Z. Hauschild, T. Ekvall, J. Guinée, R. Heijungs, S. Hellweg, A. Koehler, D. Pennington and S. Suh (2009). Recent developments in life cycle assessment. *Journal of Environmental Management* 91(1): 1-21.

Finnveden, G. and A. Moberg (2005). Environmental systems analysis tools - an overview. *Journal of Cleaner Production* 13(12): 1165-1173.

Fogelberg, H. and B. A. Sandén (2008). Understanding reflexive systems of innovation: An analysis of swedish nanotechnology discourse and organization. *Technology Analysis & Strategic Management* 20(1): 65 - 81.

Foss Hansen, S., B. H. Larsen, S. I. Olsen and A. Baun (2007). Categorization framework to aid hazard identification of nanomaterials. *Nanotoxicology* 1(3): 243 - 250.

Friedlander, S. K. (1977). *Smoke, dust and haze, fundamentals of aerosol behavior*. New York: John Wiley & Sons, Inc.

Friends of the Earth (2006). *Nanomaterials, sunscreens and cosmetics: Small ingredients, big risks*. Report by Friends of the Earth.

Friends of the Earth (2007). *Nanotechnology & sunscreens - a consumer guide for avoiding nano-sunscreens*. Report by Friends of the Earth.

Gallopín, G. C. (1996). Environmental and sustainability indicators and the concept of situational indicators. A systems approach. *Environmental Modeling and Assessment* 1: 101-117.

Geranio, L., M. Heuberger and B. Nowack (2009). The behavior of silver nanotextiles during washing. *Environmental Science & Technology* 43(21): 8113-8118.

González, S., M. Fernández-Lorente and Y. Gilaberte-Calzada (2008). The latest on skin photoprotection. *Clinics in Dermatology* 26(6): 614-626.

Gottschalk, F., C. Ort, R. W. Scholz and B. Nowack (2011). Engineered nanomaterials in rivers – exposure scenarios for switzerland at high spatial and temporal resolution. *Environmental Pollution* 159(12): 3439-3445.

Gottschalk, F., T. Sonderer, R. W. Scholz and B. Nowack (2009). Modeled environmental concentrations of engineered nanomaterials (TiO<sub>2</sub>, ZnO, Ag, CNT, fullerenes) for different regions. *Environmental Science & Technology* 43(24): 9216-9222.

Grant, S. B., J. H. Kim and C. Poor (2001). Kinetic theories for the coagulation and sedimentation of particles. *Journal of Colloid and Interface Science* 238(2): 238-250.

- Grieger, K. D., S. F. Hansen, P. B. Sørensen and A. Baun (2011). Conceptual modeling for identification of worst case conditions in environmental risk assessment of nanomaterials using nzvi and C60 as case studies. *Science of The Total Environment* 409(19): 4109-4124.
- Grubb, G. F. and B. R. Bakshi (2011). Life cycle of titanium dioxide nanoparticle production. *Journal of Industrial Ecology* 15(1): 81-95.
- Grübler, A. (1996). Time for a change: On the patterns of diffusion of innovation. *Daedalus* 125(3): 19-42.
- Grübler, A. (1998). *Technology and global change*. Cambridge: Cambridge University Press.
- Grübler, A. and N. Nakićenović (1991). *Evolution of transport systems: Past and future*. Laxenburg, Austria: International Institute for Applied Systems Analysis.
- Handy, R., F. von der Kammer, J. Lead, M. Hassellöv, R. Owen and M. Crane (2008). The ecotoxicology and chemistry of manufactured nanoparticles. *Ecotoxicology* 17(4): 287-314.
- Harremoës, P., D. Gee, M. MacGarvin, A. Stirling, J. Keys, b. Wynne and S. Guedes Vas (2001). *Late lessons from early warnings: The precautionary principle 1896-2000*. Copenhagen: European Environment Agency.
- Harte, J. (1988). *Consider a spherical cow: A course in environmental problem solving*. Sausalito: University Science Books.
- Hendren, C. O., X. Mesnard, J. Dröge and M. R. Wiesner (2011). Estimating production data for five engineered nanomaterials as a basis for exposure assessment. *Environmental Science & Technology* 45(7): 2562-2569.
- Hillman, K. M. and B. A. Sandén (2008). Time and scale in life cycle assessment: The case of fuel choice in the transport sector. *International Journal of Alternative Propulsion* 2: 1-12.
- Holmberg, J., K.-H. Robèrt and K.-E. Eriksson (1996). Socio-ecological principles for a sustainable society - scientific background and swedish experiences. *Getting down to earth: Practical applications for ecological economics*. R. Costanza. Washington DC: Island Press.
- Hong, S. J., Y. S. Choi, K. R. Kim, J. G. Kang, G. J. Oh and T. Hur (2011). Material flow analysis of paper in Korea. Part I. Data calculation model from the flow relationships between paper products. *Resources Conservation and Recycling* 55(12): 1206-1213.
- Hsu, L.-Y. and H.-M. Chein (2007). Evaluation of nanoparticle emission for TiO<sub>2</sub> nanopowder coating materials. *Nanotechnology and occupational health*: 157-163.
- Ingelstam, L. (2002). *System - att tänka över samhälle och teknik (Systems - to think over society and technology)*. Kristianstad: Swedish Energy Agency.
- ISO (2008). *Nanotechnologies — terminology and definitions for nano-objects — nanoparticle, nanofibre and nanoplate: ISO/TS 27687:2008(E)*.

- Jager, T. (2012). Bad habits die hard: The NOEC's persistence reflects poorly on ecotoxicology. *Environmental Toxicology and Chemistry* 31(2): 228-229.
- Jiang, J., G. Oberdörster and P. Biswas (2009). Characterization of size, surface charge, and agglomeration state of nanoparticle dispersions for toxicological studies. *Journal of Nanoparticle Research* 11(1): 77-89.
- Johnson, A. C., M. J. Bowes, A. Crossley, H. P. Jarvie, K. Jurkschat, M. D. Jürgens, A. J. Lawlor, B. Park, P. Rowland, D. Spurgeon, C. Svendsen, I. P. Thompson, R. J. Barnes, R. J. Williams and N. Xu (2011). An assessment of the fate, behaviour and environmental risk associated with sunscreen TiO<sub>2</sub> nanoparticles in UK field scenarios. *Science of The Total Environment* 409(13): 2503-2510.
- Ju-Nam, Y. and J. R. Lead (2008). Manufactured nanoparticles: An overview of their chemistry, interactions and potential environmental implications. *Science of The Total Environment* 400(1-3): 396-414.
- Kaegi, R., B. Sinnet, S. Zuleeg, H. Hagendorfer, E. Mueller, R. Vonbank, M. Boller and M. Burkhardt (2010). Release of silver nanoparticles from outdoor facades. *Environmental Pollution* 158(9): 2900-2905.
- Kaegi, R., A. Ulrich, B. Sinnet, R. Vonbank, A. Wichser, S. Zuleeg, H. Simmler, S. Brunner, H. Vonmont, M. Burkhardt and M. Boller (2008). Synthetic TiO<sub>2</sub> nanoparticle emission from exterior facades into the aquatic environment. *Environmental Pollution* 156(2): 233-239.
- Kahru, A. and H. C. Dubourguier (2010). From ecotoxicology to nanoecotoxicology. *Toxicology* 269(2-3): 105-119.
- Kaplan, S. and B. J. Garrick (1981). On the quantitative definition of risk. *Risk Analysis* 1(1): 11-27.
- Kapur, A., G. Keoleian, A. Kendall and S. E. Kesler (2008). Dynamic modeling of in-use cement stocks in the United States. *Journal of Industrial Ecology* 12(4): 539-556.
- Klaine, S. J., P. J. J. Alvarez, G. E. Batley, T. F. Fernandes, R. D. Handy, D. Y. Lyon, S. Mahendra, M. J. McLaughlin and J. R. Lead (2008). Nanomaterials in the environment: Behaviour, fate, bioavailability, and effects. *Environmental Toxicology and Chemistry* 27(9): 1825-1851.
- Klir, G. J. (1991). *Facets of systems science*. New York: Plenum Press.
- Kohler, A. R., C. Som, A. Helland and F. Gottschalk (2008). Studying the potential release of carbon nanotubes throughout the application life cycle. *Journal of Cleaner Production* 16(8-9): 927-937.
- Kortenkamp, A. (2007). Ten years of mixing cocktails: A review of combination effects of endocrine-disrupting chemicals. *Environmental Health Perspectives* 115: 98-105.
- Kortenkamp, A., T. Backhaus and M. Faust (2009). *State of the art report on mixture toxicity*. Brussels: European Commission.

- Kushnir, D. and B. A. Sandén (2008). Energy requirements of carbon nanoparticle production. *Journal of Industrial Ecology* 12: 360-375.
- Kwonpongsagoon, S., H. P. Bader and R. Scheidegger (2007). Modelling cadmium flows in australia on the basis of a substance flow analysis. *Clean Technologies and Environmental Policy* 9(4): 313-323.
- Lavoisier, A. (1789). *Traité élémentaire de chimie, présenté dans un ordre nouveau et d'après les découvertes modernes*. Paris: Chez Cuchet.
- Lenikan, J. and W. W. Fletcher (1977). *The chemical environment*. New York: Academic press.
- Li, B. and W.-H. Zhong (2011). Review on polymer/graphite nanoplatelet nanocomposites. *Journal of Materials Science* 46(17): 5595-5614.
- Li, X. and J. J. Lenhart (2012). Aggregation and dissolution of silver nanoparticles in natural surface water. *Environmental Science & Technology* 46(10): 5378-5386.
- Lindhe, A., L. Rosén, T. Norberg and O. Bergstedt (2009). Fault tree analysis for integrated and probabilistic risk analysis of drinking water systems. *Water Research* 43(6): 1641-1653.
- Liu, J. and R. H. Hurt (2010). Ion release kinetics and particle persistence in aqueous nano-silver colloids. *Environmental Science & Technology* 44(6): 2169-2175.
- Lubick, N. (2008). Risks of nanotechnology remain uncertain. *Environmental Science & Technology* 42(6): 1821-1824.
- Lundin, M., M. Bengtsson and S. Molander (1999). Life cycle assessment of wastewater systems: Influence of system boundaries and scale on calculated environmental loads. *Environmental Science & Technology* 34(1): 180-186.
- Luoma, S. N. (2008). *Silver nanotechnologies and the environment: Old problems or new challenges?* Washington DC: Woodrow Wilson International Center for Scholars, Project on Emerging Nanotechnologies and The PEW Charitable Trusts.
- Löfstedt, R. (2011). Risk versus hazard - how to regulate in the 21st century. *European Journal of Risk Regulation* 2: 149-168.
- Lövestam, G., H. Rauscher, G. Roebben, B. Sokull Klüttgen, N. Gibson, J.-P. Putaud and H. Stamm (2010). *Considerations on a definition of nanomaterials for regulatory purposes*. Luxembourg: Joint Research Center of the European Commission.
- Ma, X., J. Geiser-Lee, Y. Deng and A. Kolmakov (2010). Interactions between engineered nanoparticles (enps) and plants: Phytotoxicity, uptake and accumulation. *Science of The Total Environment* 408(16): 3053-3061.
- Mackay, D. (1991). *Multimedia environmental models: The fugacity approach*. Lewis Publishing: Chelsea.

- Mackay, D., A. Di Guardo, S. Paterson and C. E. Cowan (1996). Evaluating the environmental fate of a variety of types of chemicals using the eqc model. *Environ Toxicol Chem* 15(9): 1627-1637.
- Mackay, D., S. Paterson and W. Y. Shiu (1992). Generic models for evaluating the regional fate of chemicals. *Chemosphere* 24(6): 695-717.
- MacLeod, M., M. Scheringer, T. E. McKone and K. Hungerbuhler (2010). The state of multimedia mass-balance modeling in environmental science and decision-making. *Environmental Science & Technology* 44(22): 8360-8364.
- Maynard, A. D. (2011). Don't define nanomaterials. *Nature* 475(7354): 31-31.
- Maynard, A. D., R. J. Aitken, T. Butz, V. Colvin, K. Donaldson, G. Oberdorster, M. A. Philbert, J. Ryan, A. Seaton, V. Stone, S. S. Tinkle, L. Tran, N. J. Walker and D. B. Warheit (2006). Safe handling of nanotechnology. *Nature* 444(7117): 267-269.
- Mill, T. (1993). Environmental chemistry. *Ecological risk assessment*. G. W. Suter. Chelsea: Lewis Publishers.
- Miser, H. J. and E. S. Quade (1985). The context, nature and use of systems analysis. *Handbook of systems analysis. Volume one - overview of uses, procedures, applications, and practices*. H. J. Miser and E. S. Quade. Chichester: John Wiley & Sons.
- Miser, H. J. and E. S. Quade (1988a). Introduction - craftsmanship in analysis. *Handbook of systems analysis. Volume three - craft issues and procedural choices*. H. J. Miser and E. S. Quade. Chichester: John Wiley & Sons.
- Miser, H. J. and E. S. Quade (1988b). Validation. *Handbook of systems analysis. Volume three - craft issues and procedural choices*. H. J. Miser and E. S. Quade. Chichester: John Wiley & Sons.
- Movahedi, A. (2008). *Risk assessment of nanoparticle release from the structure of polymeric nanocomposites*. Gothenburg: Department of Chemical and Biological Engineering, Chalmers University of Technology.
- Mudunkotuwa, I. A. and V. H. Grassian (2011). The devil is in the details (or the surface): Impact of surface structure and surface energetics on understanding the behavior of nanomaterials in the environment. *Journal of Environmental Monitoring* 13(5): 1135-1144.
- Mueller, N. C. and B. Nowack (2008). Exposure modeling of engineered nanoparticles in the environment. *Environmental Science & Technology* 42(12): 4447-4453.
- Musee, N. (2011). Simulated environmental risk estimation of engineered nanomaterials: A case of cosmetics in Johannesburg city. *Human & Experimental Toxicology* 30(9): 1181-1195.
- Nel, A., T. Xia, L. Madler and N. Li (2006). Toxic potential of materials at the nanolevel. *Science* 311(5761): 622-627.

Nohynek, G. J., J. Lademann, C. Ribaud and M. S. Roberts (2007). Grey goo on the skin? Nanotechnology, cosmetic and sunscreen safety. *Critical Reviews in Toxicology* 37(3): 251 - 277.

Nowack, B. (2010). Nanosilver revisited downstream. *Science* 330(6007): 1054-1055.

Nowack, B., H. F. Krug and M. Height (2011). 120 years of nanosilver history: Implications for policy makers. *Environmental Science & Technology* 45(4): 1177-1183.

O'Brien, N. and E. Cummins (2008). Recent developments in nanotechnology and risk assessment strategies for addressing public and environmental health concerns. *Hum Ecol Risk Assess* 14(3): 568 - 592.

O'Brien, N. and E. Cummins (2010). Nano-scale pollutants: Fate in Irish surface and drinking water regulatory systems. *Human and Ecological Risk Assessment: An International Journal* 16(4): 847-872.

Oberdörster, G., E. Oberdörster and J. Oberdörster (2005). Nanotoxicology: An emerging discipline evolving from studies of ultrafine particles. *Environmental Health Perspectives* 113(7): 823-839.

Owen, R. and R. Handy (2007). Viewpoint: Formulating the problems for environmental risk assessment of nanomaterials. *Environmental Science & Technology* 41(16): 5582-5588.

Owens, J. W. (1997). Life-cycle assessment in relation to risk assessment: An evolving perspective. *Risk Analysis* 17(3): 359-365.

Patton, D. E. (1993). The ABCs of risk assessment. *EPA Journal* 19: 10-15.

Pistocchi, A., D. A. Sarigiannis and P. Vizcaino (2010). Spatially explicit multimedia fate models for pollutants in Europe: State of the art and perspectives. *Science of The Total Environment* 408(18): 3817-3830.

Poland, C. A., R. Duffin, I. Kinloch, A. Maynard, W. A. H. Wallace, A. Seaton, V. Stone, S. Brown, W. MacNee and K. Donaldson (2008). Carbon nanotubes introduced into the abdominal cavity of mice show asbestos-like pathogenicity in a pilot study. *Nat Nano* 3(7): 423-428.

Posthuma, L., G. W. Suter and T. P. Traas (2002). *Species sensitivity distributions in ecotoxicology*. Boca Raton: Lewis Publishers.

Praetorius, A., M. Scheringer and K. Hungerbühler (2012). Development of environmental fate models for engineered nanoparticles—a case study of TiO<sub>2</sub> nanoparticles in the Rhine river. *Environmental Science & Technology*.

Project on Emerging Nanotechnologies (2012).  
[http://www.nanotechproject.org/inventories/consumer/analysis\\_draft/](http://www.nanotechproject.org/inventories/consumer/analysis_draft/).

- Qiao, M., Y. M. Zheng and Y. G. Zhu (2011). Material flow analysis of phosphorus through food consumption in two megacities in northern China. *Chemosphere* 84(6): 773-778.
- Quik, J. T. K., M. C. Stuart, M. Wouterse, W. Peijnenburg, A. J. Hendriks and D. van de Meent (2012). Natural colloids are the dominant factor in the sedimentation of nanoparticles. *Environmental Toxicology and Chemistry* 31(5): 1019-1022.
- Quik, J. T. K., J. A. Vonk, S. F. Hansen, A. Baun and D. Van De Meent (2011). How to assess exposure of aquatic organisms to manufactured nanoparticles? *Environment International* 37(6): 1068-1077.
- Renn, O. (1998). Three decades of risk research: Accomplishments and new challenges. *Journal of Risk Research* 1: 49-71.
- Roco, M. C. (2004). Nanoscale science and engineering: Unifying and transforming tools. *AIChE Journal* 50(5): 890-897.
- Royal Society (2004). *Nanoscience and nanotechnologies: Opportunities and uncertainties*: London.
- Sandén, B. A. (2004). Technology path assessment for sustainable technology development. *Innovation: management, policy and practice* 6: 316-330.
- Sandén, B. A. (2008). Standing the test of time: Signals and noise from environmental assessments of energy technologies. Materials Research Society Symposium Proceedings.
- Sanderson, K. D., S. Hurst, T. McKittrick, D. Rimmer and L. Ye (2003). Photocatalytic coatings for self cleaning glass. Glass Processing Days, Tampere, Finland.
- Santillo, D. and P. Johnston (1999). Is there a role for risk assessment within precautionary legislation? *Human and Ecological Risk Assessment* 5(5): 923-932.
- Scheringer, M. and M. Berg (1994). Spatial and temporal range as measures of environmental threat. *Fresenius Environmental Bulletin* 3: 493-498.
- Schlesinger, W. H. (1991). *Biogeochemistry: An analysis of global change*. San Diego: Academic Press.
- Schmidt, K. F. (2007). *Green nanotechnology: It's easier than you think*. Washington DC: Woodrow Wilson International Center for Scholars, Project on Emerging Nanotechnologies and The PEW Charitable Trusts.
- Segal, M. (2009). Selling graphene by the ton. *Nature Nanotechnology* 4(10): 612-614.
- Serpone, N., D. Dondi and A. Albini (2007). Inorganic and organic UV filters: Their role and efficacy in sunscreens and suncare product. *Inorganica Chimica Acta* 360(3): 794-802.
- Shaw, D. J. (1992). *Introduction to colloid and surface chemistry*. Oxford: Elsevier Science Ltd.

Silver, S., L. Phung and G. Silver (2006). Silver as biocides in burn and wound dressings and bacterial resistance to silver compounds. *Journal of Industrial Microbiology and Biotechnology* 33(7): 627-634.

Slovic, P. (2000). *The perception of risk*. London: Earthscan Publications Ltd.

Slovic, P. (2002). Terrorism as hazard: A new species of trouble. *Risk Analysis* 22(3): 425-426.

Smil, V. (1985). *Carbon-nitrogen-sulfur: Human interference in grand biospheric cycles*. New York: Plenum Press.

Smoluchowski, M. (1917). Versuch einer mathematischen Theorie der Koagulationskinetic Kolloider Lösungen. *Zeitschrift für Physikalische Chemie* 92: 129-168.

Stephan, C. E. (1986). Proposed goal of applied aquatic toxicology. *Aquatic toxicology and environmental fate (ninth volume)*. Stp 921. T. M. Poston and R. Purdy. Philadelphia: American Society for Testing and Materials International.

Steubing, B., H. Boni, M. Schlupe, U. Silva and C. Ludwig (2010). Assessing computer waste generation in Chile using material flow analysis. *Waste Management* 30(3): 473-482.

Subramanian, V., J. Youtie, A. Porter and P. Shapira (2010). Is there a shift to “active nanostructures”? *Journal of Nanoparticle Research* 12(1): 1-10.

Suter, G. W. (1989). Ecological endpoints. *Ecological assessment of hazardous waste sites: A field and laboratory reference document*. Epa 600/3-89/013. W. Warren-Hicks, B. R. Parkhurst and S. S. Baker. Oregon: Corvallis Environmental Research Laboratory.

Suter, G. W. (1993a). *Ecological risk assessment*. Chelsea: Lewis Publishers.

Suter, G. W. (1993b). Exposure. *Ecological risk assessment*. G. W. Suter. Chelsea: Lewis Publishers.

Suter, G. W. (1993c). Predictive risk assessment of chemicals. *Ecological risk assessment*. G. W. Suter. Chelsea: Lewis Publishers.

Suter, G. W. and L. W. Barnhouse (1993). Assessment concepts. *Ecological risk assessment*. G. W. Suter. Chelsea: Lewis Publishers.

Swedish Chemicals Agency (2011). *Antibakteriella ämnen läcker från kläder vid tvätt - analys av silver, triklosan och triklokarban i textilier före och efter tvätt (Antibacterial substances leach from clothes during washing - analysis of silver, triclosan and triclocarban in textiles before and after washing)*. Sundbyberg: PM 4/11.

Swedish Environmental Protection Agency (1997). *Development of generic guideline values. Model and data used for generic guideline values for contaminated soils in Sweden*. Stockholm: Report No. 4639.



Sweet, L. and B. Strohman (2006). Nanotechnology—life-cycle risk management. *Human and Ecological Risk Assessment: An International Journal* 12(3): 528 - 551.

Thompson, M., R. Ellis and A. Wildavsky (1990). *Cultural theory*. Boulder, Colorado: Westview.

Tour, J. M. (2007). Nanotechnology: The passive, active and hybrid sides - gauging the investment landscape from the technology perspective. *Nanotechnology law & Business* 4(3): 361-373.

Traas, T. P. and C. J. van Leeuwen (2007). Ecotoxicological effects. *Risk assessment of chemicals: An introduction*. C. J. van Leeuwen and T. Vermeire. Dordrecht: Springer.

United Nations (1992). *Environmentally sound management of toxic chemicals including prevention of illegal international traffic in toxic and dangerous products. Agenda 21, chapter 19*. Rio de Janeiro: United Nations Conference on Environment and Development.

USEPA (1998). *Guidelines for ecological risk assessment*: Washington DC.

van de Meent, D. and J. H. M. Bruijn (2007). Environmental exposure assessment. *Risk assessment of chemicals: An introduction*. C. J. van Leeuwen and T. G. Vermeire. Dordrecht: Springer.

van der Voet, E. (2002). Substance flow analysis methodology. *A handbook of industrial ecology*. R. U. Ayres and L. W. Ayres. Cheltenham: Edward Elgar.

van der Voet, E., L. van Oers, J. B. Guinee and H. A. U. de Haes (1999). Using SFA indicators to support environmental policy. *Environmental Science and Pollution Research* 6(1): 49-58.

van Hoecke, K., K. A. C. De Schampelaere, P. Van der Meeren, S. Lucas and C. R. Janssen (2008). Ecotoxicity of silica nanoparticles to the green alga *Pseudokirchneriella subcapitata*: Importance of surface area. *Environmental Toxicology and Chemistry* 27(9): 1948-1957.

van Leeuwen, C. J. and T. G. Vermeire (2007). *Risk assessment of chemicals: An introduction*. Dordrecht: Springer.

Verwey, E. J. W. and J. T. G. Overbeek (1948). *Theory of the stability of lyophobic colloids*. Amsterdam: Elsevier.

Wiesner, M. R. (1992). Kinetics of aggregate formation in rapid mix. *Water Research* 26(3): 379-387.

Wiesner, M. R., G. V. Lowry, K. L. Jones, J. M. F. Hochella, R. T. Di Giulio, E. Casman and E. S. Bernhardt (2009). Decreasing uncertainties in assessing environmental exposure, risk, and ecological implications of nanomaterials. *Environmental Science & Technology* 43(17): 6458-6462.

Wijnhoven, S. W. P., W. J. G. M. Peijnenburg, C. A. Herberts, W. I. Hagens, A. G. Oomen, E. H. W. Heugens, B. Roszek, J. Bisschops, I. Gosens, D. Van De Meent, S. Dekkers, W. H.

De Jong, M. van Zijverden, A. J. A. M. Sips and R. E. Geertsma (2009). Nano-silver – a review of available data and knowledge gaps in human and environmental risk assessment. *Nanotoxicology* 3(2): 109 - 138.

Williams, R. J., M. D. Jürgens and A. C. Johnson (1999). Initial predictions of the concentrations and distribution of 17 beta-oestradiol, oestrone and ethinyl oestradiol in 3 english rivers. *Water Research* 33(7): 1663-1671.

Williams, R. J., V. D. J. Keller, A. C. Johnson, A. R. Young, M. G. R. Holmes, C. Wells, M. Gross-Sorokin and R. Benstead (2009). A national risk assessment for intersex in fish arising from steroid estrogens. *Environmental Toxicology and Chemistry* 28(1): 220-230.

Zhang, W., J. Crittenden, K. Li and Y. Chen (2012). Attachment efficiency of nanoparticle aggregation in aqueous dispersions: Modeling and experimental validation. *Environmental Science & Technology*.

Zweers, P. G. P. C. and T. G. Vermeire (2007). Data: Needs, availability, sources and evaluation. *Risk assessment of chemicals: An introduction*. C. J. van Leeuwen and T. G. Vermeire. Dordrecht: Springer.