Review

Finding Nano: Challenges Involved in Monitoring the Presence and Fate of Engineered Titanium Dioxide Nanoparticles in Aquatic Environments

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Abstract: In recent years, titanium dioxide (TiO₂) has increasingly been used as an inorganic ultraviolet (UV) filter for sun protection. However, nano-TiO₂ may also pose risks to the health of humans and the environment. Thus, to adequately assess its potential adverse effects, a comprehensive understanding of the behaviour and fate of TiO₂ in different environments is crucial. Advances in analytical and modelling methods continue to improve researchers' ability to quantify and determine the state of nano-TiO₂ in various environments. However, due to the complexity of environmental and nanoparticle factors and their interplay, this remains a challenging and poorly resolved feat. This paper aims to provide a focused summary of key particle and environmental characteristics that influence the behaviour and fate of sunscreen-derived TiO₂ in swimming pool water and natural aquatic environments and to review the current state-of-the-art of single particle inductively coupled plasma mass spectrometry (SP-ICP-MS) approaches to detect and characterise TiO₂ nanoparticles in aqueous media. Furthermore, it critically analyses the capability of existing fate and transport models to predict environmental TiO₂ levels. Four particle and environmental key factors that govern the fate and behaviour of TiO₂ in aqueous environments are identified. A comparison of SP-ICP-MS studies reveals that it remains challenging to detect and characterise engineered TiO₂ nanoparticles in various matrices and highlights the need for the development of new SP-ICP-MS pre-treatment and analysis approaches. This review shows that modelling studies are an essential addition to experimental studies, but they still lack in spatial and temporal resolution and mostly exclude surface transformation processes. Finally, this study identifies the use of Bayesian Network-based models as an underexplored but promising modelling tool to overcome data uncertainties and incorporates interconnected variables.

Keywords: nano-TiO₂; inorganic UV filter; sunscreen; surface coating deterioration; SP-ICP-MS; fate and transport modelling; risk assessment; Bayesian network; aquatic pollution

1. Introduction

Skin cancer (melanoma and non-melanoma) is one of the most common cancer types worldwide [1,2]. To reduce the risks of it, public awareness campaigns that promote the importance of the use of broad-spectrum (280–400 nm) ultraviolet radiation (UVR) protection have increased over the last few decades. These campaigns have been encouraging the use of sunscreen as an important protection measure. As a result, the use of sunscreen globally has increased significantly. For example, due to the Australian campaign 'SunSmart', sunscreen use has risen by 25% over the past 30 years [3].

However, with the increased application of sunscreen, there are concerns regarding the inevitable release and environmental consequences of sunscreen residues. These concerns are further cemented because the full extent of potential environmental consequences has not yet been clarified. Based on the risks to human and environmental health, some governments have started introducing national bans on certain organic ultraviolet (UV) filters [4]. Subsequently, inorganic UV filters such as titanium dioxide (TiO₂) or zinc oxide (ZnO) gained popularity as the 'reef-safe' and 'eco-friendly' alternatives. However, there is a continued debate on whether inorganic UV filters, especially in nanoparticle (NP) form, are safe to use or whether they pose a risk to humans and the environment, particularly when used for longer periods.

Sobek et al. [5] classified TiO₂ as toxic to aquatic life with long-lasting effects based on the regulation on classification, labelling, and packaging (CLP) of substances and mixtures. Furthermore, the International Agency for Research on Cancer [6] has categorised TiO₂ as possibly carcinogenic (Group 2B).

Besides being potentially cytotoxic and genotoxic [7,8], TiO₂ is a known photocatalyst and is capable of generating reactive oxygen species (ROS) such as hydrogen peroxide (H₂O₂), hydroxyl radicals (OH·), or singlet oxygen (¹O₂). This is another drawback of TiO₂, as ROS can induce oxidative stress and catalyse DNA damage [9,10]. To reduce the catalytic activity, recent studies have been focusing on reducing the ROS production by either doping with other elements or by coating the synthesised NP [11]. However, previous studies have shown that these coatings can (partially) deteriorate when subject to some exposure conditions [12,13], affecting both the degree of toxicity and the fate of the environmental.

Even though the number of (eco-)toxicity studies has substantially increased over the last few decades, experimental studies that conduct long-term investigations are still limited [14] and rarely consider real environmental conditions as an exposure scenario [15]. Furthermore, Minetto et al. [15] reported that, as studies do not follow a standardised experimental procedure, results are rarely comparable and reproducible. Study outcomes of the same core material may also be inconsistent due to the effect of different particle properties, such as particle size (PS), shape, surface coating on the (eco-)toxicity, and the different NP behaviour in various environmental or laboratory settings [16,17]. A recent study published in 2021 reports that solar radiation significantly increases the ecotoxicity of nano-TiO₂ in aquatic environments, particularly if organic UV filters are simultaneously present [18]. Consequently, eco-toxicologists need a better understanding of the particle behaviour to interpret the results appropriately and to develop innovative toxicity studies.

In addition to the common eco-toxicological dose descriptors, more behavioural toxicological endpoints are needed to identify potential risks; for example, the exposure to TiO₂ caused substantial disruptions in the swimming behaviour of clownfish, whereas their mortality rate only slightly increased [19]. Another aspect that is understudied is the effect of chronic exposure to by-products of aged nano-TiO₂ in aquatic organisms. For instance, Fouqueray et al. [20] observed a decrease in growth and reproduction of *Daphnia Magna* that was fed nano-TiO₂ residue-contaminated algae over 21 days. Such observations also raise concerns regarding the potential for trophic transfer and bioaccumulation in the food chain.

Based on a literature search, algae were the most vulnerable group of aquatic organisms when exposed to nano-TiO₂ with a no observed effect concentration (NOEC) of <0.2 mg TiO₂/L [21]. The NOEC can be converted to the predicted no-effect concentration (PNEC) by dividing the NOEC by an assessment factor (AF). Estimates of the PNEC are essential for carrying out an environmental risk assessment (ERA). Due to the limited number of long-term studies, applying an AF of 100–1000 is considered conservative and reasonable [22]. Based on these estimates, the PNEC value is 0.2–2 µg/L, which is consistent with the findings of previous studies, which have produced values such as 1 µg/L [23], 16 µg/L [24], and 20 µg/L [25].

Besides the PNEC value, a precise determination of the predicted environmental concentration (PEC) of nano-TiO₂ is essential for an accurate ERA. The PEC can be derived from both analytical and modelling studies; however, neither approach has, so far, been able to resolve the variability of PEC in different environments in detail [26]. This can partly be attributed to challenges associated with appropriate and robust analytical methods but also to the complexity and breadth of this emergent field. As analytical techniques are not able to explain all real-scenario observations, modelling approaches are considered a critical and complementary tool to fill the knowledge gaps [27]. Understanding the behaviour of nano-TiO₂ in diverse environments is important for building a robust model. However, this can rarely be done through analytical studies, and, therefore, it necessitates hybrid approaches to overcome these challenges.

This review aims to address these challenges by (1) identifying potential exposure pathways of nano-TiO₂ to the environment; (2) discussing the impact of individual particles and environmental factors on the fate and behaviour of nano-TiO₂; (3) reviewing relevant experimental studies that examined the fate and behaviour processes of nano-TiO₂ in selected environmental compartments; (4) analysing the suitability of single particle inductively coupled plasma mass spectrometry (SP-ICP-MS) to measure nano-TiO₂ in the environment; and (5) evaluating the potential use of modelling methods to support analytical approaches.

It should be noted that nano-TiO₂ is released into the hydrosphere from multiple sources and poses a potentially serious risk to aquatic environments. Although this review mainly focuses on TiO₂ released from sunscreens, it also discusses the recent developments in approaches and techniques for identifying and monitoring the presence and fate of engineered nano-TiO₂, which has relevance to researchers seeking better understanding of nano-TiO₂ from these varied contributing sources.

2. Distribution and Fate of Nano-TiO₂ in the Environment

Owing to its unique properties, nano-TiO₂ is applied widely, including to cosmetics (59%), paint and coatings (13%), electronics (7%), cleaning agents (6%), filters (6%), plastics (4%), and wastewater (WW) disinfectants (<1%) [28]. It is estimated that sunscreens make up about 25% of the nano-TiO₂ market share [29]. Consequently, sunscreens are likely to be one of the significant sources of nano-TiO₂ released into the environment.

2.1. Exposure Pathways to the Environment

To evaluate the environmental risk of nano-TiO₂ in sunscreen, it is helpful to determine the potential input and distribution channels. Figure 1 illustrates the exposure pathways of nano-TiO₂ from sunscreens to the environment. The release of nano-TiO₂ into aqueous environments is likely to occur once users enter the water after applying sunscreen. Depending on the viscosity of the formulation, 10–40% of NPs are released from the initially applied sunscreen [30].

The remaining nano-TiO₂ residues enter the WW stream after being washed off in the shower. In the WW treatment plants (WWTPs), it is estimated that, on average, approximately 34% and 87% of nano-TiO₂ is removed from the primary and secondary settling tanks, respectively [31]. However, since sewage sludge is often used as soil fertiliser, nano-TiO₂ could contaminate agricultural soils and may even leach into the groundwater, consequently re-entering the aqueous environment [32,33]. The leaching behaviour greatly depends on the nature of the soil and has not been studied adequately [14,34]. In one study, Dulger et al. [35] investigated the leaching potential of nano-TiO₂ in landfills and concluded that about 81–97% of the introduced nano-TiO₂ is retained on the solid surface. However, to date, the extent to which nano-TiO₂ leaches from sewage sludge remains unclear.

Another exposure pathway that is only occasionally considered in the literature is the washing off of sunscreen during activities in swimming pool water (SPW). However, this should be considered as part of realistic and regionalised calculations as the number of privately owned swimming pools continues to increase steadily. For example, in Australia,

residential pool ownership has risen from 12% to 13% over the last three years [36], and it is expected that sunscreen is used as most of these swimming pools are outdoors. Therefore, nano-TiO₂ released from sunscreen is likely to be found in (1) diverse aqueous media (e.g., SPW, natural waters); (2) WWTPs; (3) sewage sludge; (4) agriculture soils; and (5) landfill. This review paper primarily focuses on the fate and behaviour of nano-TiO₂ in the first of these environments, the aqueous media.

Figure 1. Routes of entry of nano-TiO₂ contained in sunscreens into the environment; adopted from Musee [23]. The grey boxes represent the focus of this research.

2.2. Behaviour and Fate of Nano-TiO₂

Understanding the particle behaviour and fate of nano-TiO₂ helps to predict its concentration and state in the environment, which then determine the risk and impact on the environment. The following three sections discuss the influence of selected nano-TiO₂ properties and environmental conditions on the particle behaviour and fate and conclude with an overview of experimental research findings.

2.2.1. The Pivotal Role of Nano-TiO₂ Characteristics

Commercially available nano-TiO₂ suitable for incorporating into sunscreen formulas varies in its characteristics such as PS, shape, crystalline phase, core composition, and surface properties. These physicochemical properties can significantly affect the behaviour, fate, and (eco)toxicity of nano-TiO₂ as discussed below.

Due to manufacturing processes, the PS of TiO₂ can vary in precision and accuracy, and thus, is usually high in polydispersity that may extend beyond the nanometre scale. However, the PS for obtaining a transparent sunscreen with adequate UV attenuation typically ranges from 10–40 nm [37,38]. An increase in PS shifts the UV attenuation capability

of TiO₂ to longer wavelengths, and, hence, influences the range of UV protection [39]. Therefore, to maintain the desired UV attenuation, the tendency of smaller particles to form aggregates and agglomerates should be prevented [40]. However, smaller particles exhibit higher toxicity [41] and are even able to penetrate human skin and enter the bloodstream [42]. Similarly, Pelclova et al. [43] detected nano-TiO₂ (<14 nm) in biological fluids such as plasma and urine due to the absorption of nano-TiO₂ through the human skin. Moreover, the photocatalytic activity of TiO₂ is size-dependent as a result of charge-carrier dynamics, light absorption and scattering efficiency, as well as the specific surface area [44].

The particle shape of nano-TiO₂ found in sunscreens varies from spherical, elongated (rod-shaped, needle-shaped) to ellipsoidal forms [45,46]. The NP shape also affects the toxicity, including by influencing the rate of particle uptake by primary human immune cells [47]. However, to date, studies reporting correlations between particle shape and environmental or human health risks are limited [48,49].

TiO₂ can exist in three crystalline forms: anatase, rutile, and brookite [32]. However, only pure forms of rutile or anatase or a mixture of both are incorporated in sunscreens [46,50]. Among other characteristics, the crystal structures determine the potential toxicity of TiO₂. For example, anatase and anatase mixtures are under suspicion of causing oxidative stress or cytotoxicity [51,52]. Despite these concerns, many sunscreens often still contain anatase [46].

The core composition of nano-TiO₂ can be altered by metal doping with, for example, manganese (Mg), vanadium (V), or iron (Fe) [32]. Variations in the core composition can change the overall physicochemical properties, and, thus, impact the holistic behaviour and fate of the NPs in the environment [53,54]. The aim of structural modifications is primarily to lower or quench the generation of ROS, which reduces the phototoxicity of nano-TiO₂ [55,56].

The surface chemistry is a key factor that influences nano-TiO₂ characteristics such as photocatalytic activity or dispersibility [57]. As smaller particles tend to aggregate readily [40], surface coatings are frequently applied to sustain particle stability in the sunscreen [58]. The formulation type of a sunscreen determines what surface treatment to use to promote dispersibility and particle stabilisation. Oil-in-water (O/W) types allow for the incorporation and stabilisation of nano-TiO₂ as is, whereas water-in-oil (W/O) types usually require organic coatings that change the hydrophilic character of the surface to a lipophilic one [59]. The photocatalytic effect has also been suppressed by applying inorganic layers such as aluminium oxide Al₂O₃, aluminium hydroxide Al(OH)₃, (hydrated) silica SiO₂, or a combination of the above [60,61] to passivate the TiO₂ surface. Additionally, they can be combined with organic surface treatments to improve the dispersibility in W/O types [62].

However, surface treatments can wear out over time and are susceptible to alteration or degradation when exposed to diverse media. Therefore, previous studies have attempted to examine the influence of extrinsic factors. For example, if hydrophobic organic or polymeric coatings such as polydimethylsiloxane (PDMS) are exposed to pH neutral ultrapure water, over time (hours to days), the PDMS layer completely dissolves and the particle surface becomes hydrophilic [63]. This promotes the dispersibility of nano-TiO₂ in aqueous environments and the formation of stable colloids. Similarly, Auffan et al. [13] observed a complete dissolution of the PDMS layer and a partial deterioration of the Al(OH)₃ layer in contact with water (pH = 5). On the contrary, Wu et al. [62] found that layers of a structurally related polymer (hydrogen dimethicone) do not dissolve in water and remain hydrophobic even after sonification. However, if 1% (v/v) organic solvent such as ethanol (EtOH) was added, the organic coating dissolved.

Nevertheless, the Al(OH)₃ layer seems to retain its protective properties when in contact with deionised (DI) water, as the coating still inhibits the generation of ROS [13]. However, if exposed to SPW or seawater, a significant redistribution of the Al(OH)₃ coating occurs [12,64]. Herein, it was found that especially chlorine (HOCl/OCl[−]) was responsible for diminishing the coating's integrity [65]. The redistribution of the Al(OH)₃ coating also

resulted in enhanced photocatalytic activity compared to unaged nano-TiO₂ [12]. According to Al-Abed et al. [12], the layer thickness is critical for the prevention of photocatalytic activities. Moreover, previous studies have indicated that UVR could also affect the integrity of the Al(OH)₃ layer [62]. The damage or loss of protective surface layers not only influences transport or fate processes but also restores the photoactivity of nano-TiO₂ [66] and is therefore undesirable.

To overcome these shortcomings and to ensure the sunscreen endures the harsh environmental conditions, new surface treatments (Table 1) have been developed in recent years. Table 1 summarises recent findings that primarily refer to novel organic and TiO₂ hybrid nanostructures or the incorporation of TiO₂ into inorganic auxiliary structures. Table 1 only consists of surface treatments that would seem viable for commercial use. We defined a surface treatment as viable if it had a realistic number of manufacturing process steps.

Table 1. Novel surface treatments that intend safe usage of TiO₂ as UV filter in cosmetic formulations.

Surface Treatment	Benefits	Reference
R: Chemically coated lignosulfonate	Lignin/TiO₂ nanocomposites Previous study with similar approach: Encapsulation of TiO₂ by different types of lignin [67]	Good dispersibility; high sun protection factor (SPF) [68]
CNC: Cellulose nanocrystals	Organic/TiO₂ hybrid nanostructures TiO₂ NPs grafted onto cellulose nanocrystals (CNC)	High SPF; in o/w: replaces surfactant in formulation [69]
TA: Tannic acid p-MS: porous polymer microspheres	Tannin/TiO₂ multilayers on p-MS Deposition on porous polymethylmethacrylate (PMMA) microspheres Layer-by-layer assembly of TiO₂ and TA via ligand-to-metal complexation	Reduced ROS; high SPF [70]
TiO₂	Surface functionalisation with Oxisol Oxisol: Polyphenol dihydroxyphenyl benzimidazole carboxylic acid Addition mechanism of Oxisol to TiO₂ Steric stabilisation likely	Reduced ROS; reduced photocatalytic activity; high SPF [71]
MMC: Mesoporous magnesium carbonate cluster	MMC-TiO₂-ZnO Incorporation of TiO₂ and ZnO into an amorphous MMC structure (+ dimethicone layer)	Comparable SPF; no photocatalytic activity [72]
CROSS-POLYMER silicate polyalkylsilsesquioxane polydimethylsiloxane TiO₂	TiO₂ multifunctional coating Dense and homogeneous encapsulation	Improved esthetic feel; reduced photocatalytic activity; high SPF [73]

Table 1. Cont.

	Surface Treatment	Benefits	Reference
 Y_2O_3 : Yttrium oxide	$\text{Y}_2\text{O}_3/\text{TiO}_2$ nanocomposites Deposition of Y_2O_3 onto TiO_2 Uniform Y_2O_3 coating	Enhanced UV attenuation; reduced photocatalytic activity; biocompatible	[74]
 CeO_2 : Cerium dioxide	$\text{CeO}_2/\text{TiO}_2$ nanocomposites CeO_2 nanodot encrusted TiO_2 NPs	Reduced photocatalytic activity; biocompatible	[75]

Importantly, even though new surface treatments may improve the performance of TiO_2 -based UV filters, there still remain uncertainties around their ecotoxicity and fate. Given that the surface coatings are largely responsible for the fate, exposure and hazard of nano- TiO_2 , often independently of the TiO_2 core [57], it is critical that new coatings and formulations are assessed for their (eco)toxicity before or as they become commercialised and mass-produced.

2.2.2. The Influence of Environmental Conditions

Assessing the influence of environmental factors such as pH, ionic strength (IS), and composition and occurrence of natural organic matter (NOM) is essential when evaluating the behaviour of nano- TiO_2 in real environments. The impact of these factors on the colloidal stability can often be explained by the Derjaguin-Landau-Verwey-Overbeek (DLVO) theory [76,77] that considers the combined effects of van der Waals (VDW) attraction and electrical double layer (EDL) repulsion. However, in natural environmental systems, nano- TiO_2 is likely to adsorb water molecules and macromolecules, such as NOM at the interface, which results in further interparticle forces (e.g., hydration or steric interactions). Therefore, the assessment of colloidal stability should also include non-DLVO forces. Based on experimental results (Table 2), three key factors were identified that substantially affect the behaviour of nano- TiO_2 .

Firstly, the interplay between the pH of the media and the isoelectric point (IEP) of TiO_2 significantly influences the colloidal stability of nano- TiO_2 . That is, if the pH is close to the IEP, the surface charge changes sign with only small pH variations, considerably reducing the colloidal stability due to the annihilation of electrostatic repulsion [63]. Conversely, the NPs are considered stable if the zeta potential exceeds ± 30 mV at the given pH of the environment [78].

Recent research has established that the IEPs of TiO_2 NPs extracted from commercial sunscreens were all below 4.6 [45]. As the pH in natural waters is between 6–9 [79], the surface charge of TiO_2 NP is expected to be negative. This promotes the stabilisation of nano- TiO_2 due to EDL repulsion but only if no further environmental factors affect the colloidal stability.

The IEP of TiO_2 differs depending on its crystalline structure (e.g., 3.5 for anatase and 6.5 for rutile) [80] and can change as a result of the application of additional coatings. For example, the IEP decreases if coated with SiO_2 (IEP of 2.0) or increases if coated with Al_2O_3 or $\text{Al}(\text{OH})_3$ (IEP of 9 or 6.8, respectively) [80]. These alterations can affect the fate and behaviour of nano- TiO_2 in the environment. However, as the colloidal stability not only depends on the IEP as a function of the pH but also on the general chemistry of the environment, it is assumed that the primary aim of novel coatings is to reduce the photocatalytic activity rather than to influence the IEP of nano- TiO_2 .

Nevertheless, information on both the pH and IEP in combination with other influencing factors can aid in describing and predicting the fate and behaviour of nano-TiO₂. For example, Englehart et al. [81] observed that a polymer sunscreen additive decreased the initial IEP of TiO₂ from 6.3 to less than 5, which entailed a diminished capacity of water-saturated porous media (e.g., sand) to retain nano-TiO₂ at environmentally relevant pH values.

Secondly, the IS and the type of ion also affect the colloidal stability of nano-TiO₂ in diverse environments. Zhang et al. [82] investigated the impact of ions such as Na⁺, Ca²⁺, Cl[−], and PO₄^{3−} at a high and low IS on the stability of nano-TiO₂. They observed that at a low IS the surface complexation with PO₄^{3−} contributed to an elevated negative surface charge, thus promoting the NP stability due to the electrostatic repulsion. However, with an increasing IS, the negative surface charge of nano-TiO₂ could no longer increase as the number of complexation sites on the particle surface was limited and already used up with PO₄^{3−}. Consequently, at higher IS, the high compression of the EDL can overcome the limited electrostatic repulsion, leading to a destabilisation of the nano-TiO₂. Furthermore, they observed that Na⁺ and Ca²⁺ were equally able to destabilise nano-TiO₂ at the same IS, while some cations, especially divalent cations like Ca²⁺, were able to induce bridging of two negatively charged surfaces [83] and promote the formation of aggregates.

Thirdly, the type and concentration of NOM significantly affect the colloidal stability of nano-TiO₂ as the adsorption of polymers at the interface can, for instance, lead to attractive (polymer bridging) or repulsive steric interactions. In the literature, researchers investigating the influence of different types of NOM on colloidal stability have primarily focused on fulvic (FA) and humic acids (HA). Even though both acids can adsorb onto the NP surface, the adsorption percentage of HA has been shown to be twice as much in water compared to FA due to its greater hydrophobicity [83]. Therefore, HA hindered the particle aggregation more effectively than FA. However, Luo et al.'s study observed that this only applies to media with an IS lower than the critical coagulation concentration (CCC) of nano-TiO₂. In the case of IS > CCC, the presence of HA promotes the nano-TiO₂ aggregation even more. As reported by Slomberg et al. [84], nano-TiO₂ prefers to interact with anionic NOM with high or medium molecular weights.

The assessment of the impact of NOM should always consider the whole environmental matrix, as this significantly influences the experimental outcome. At high IS, nano-TiO₂ can aggregate due to reduced repulsive forces as a result of the EDL compression [85]. However, this aggregation behaviour can be modified or reduced in the presence of NOM due to electrostatic and steric forces [83]. For example, Labille et al. [86] studied the heteroaggregation potential of TiO₂ and smectite clay considering the influence of pH, IS, and NOM. Regardless of whether the pH is above or below the IEP of the original TiO₂ NPs, the adsorption of NOM on the surface of clay and TiO₂ supports the colloidal stability even at a high IS (0.1 M NaCl). However, Luo et al. [83] observed the destabilisation of nano-TiO₂ in the presence of NOM at pH 8 > IEP and an even lower IS (>0.005 M CaCl₂), which is likely explained by the ability of Ca²⁺ ions to link two negatively charged surfaces—in this case, NOM and nano-TiO₂—and thus enhance aggregation.

2.2.3. Experimentally Observed Behaviour and Fate Processes

Having considered the key influential factors separately, this section focuses on the experimentally observed behaviour and fate processes that were described in the context of specific environments. Overall, the environmental processes (Figure 2) that dominantly affected the behaviour and fate of nano-TiO₂ were (1) transport processes (sedimentation, resuspension); (2) transformation processes (surface transformation, photolysis, homo-/heteroaggregation and/or -agglomeration); and (3) bioaccumulation (transport vector for heavy metals). Table 2 summarises the experimental findings from the past decade that help to understand the fate and behaviour of nano-TiO₂ in various matrices.

Figure 2. Schematic view of potential transformation, transport, and bioaccumulation processes in an aqueous environment.

Table 2. Overview of experimental studies that have investigated behaviour and fate processes in sunscreen, SPW, and natural aquatic environments.

Matrix	Exposure	Predominant Processes	Implication	Reference
Sunscreen	Oxybenzone, avobenzone, octyl methoxycinnamate	Photodegradation of organic UV filters	Joint toxicity	[87,88]
	Acrylates/C10-30 alkyl acrylate cross-polymer (stabilising agent)	Adsorption of the polymer, decrease IEP from 6.3 to <5	Electrostatic NP stabilization, enhanced NP mobility at environmentally relevant pH values (6–9), reduced filtration efficiency	[81]
	EtOH, UVR	Partial degradation of the hydrogen dimethicone coating due to the dissolving ability of EtOH	Photodegradation of the organic and subjacent layer: $\text{Al}(\text{OH})_3$	[62]
	Hydroxy acids (Salicylic/citric acid) Additional NPs in formulation	Biomolecular chelation of Ti^{4+}	Induced solubilization by chelation Higher phototoxicity	[8] [14]

Table 2. Cont.

Matrix	Exposure	Predominant Processes	Implication	Reference
SPW	Calcium sulphate dihydrate (CaSO ₄ • 2 H ₂ O)	Adsorption of Ca ²⁺ increased zeta potential	Reduced colloidal stability	[65]
	Chlorine	Surface transformation, redistribution of the Al(OH) ₃ protective layer	Reduced agglomeration, formation of porous aggregates, depletion of Al(OH) ₃ coating from the nano-TiO ₂ surface	[65]
		Surface transformation, redistribution of the Al(OH) ₃ protective layer	Depletion of Al(OH) ₃ coating from the nano-TiO ₂ surface, photocatalytic formation of hydroxyl radicals (•OH)	[12,64]
	Potassium cetyl phosphate (C ₁₆ H ₃₄ KO ₄ P, PCP) and chlorine	Degradation of PCP releases PO ₄ ^{3−} ions, subsequent formation of AlPO ₄ precipitates	Acceleration of protective coating depletion	[65]
		Change of physicochemical properties, e.g., smaller particles, more spherical		[64]
Natural aquatic environment		Dissolution, dominance of dissolved Ti species		[89]
	UVR, seawater	Photocatalytic reactions	Formation of hydrogen peroxide (H ₂ O ₂)	[90]
	Shear forces (induced by light, sonication)	Partial disagglomeration	Enhanced NP mobility	[91]
	Higher ambient temperature	Hydrodynamic diameter increases	Enhanced NP sedimentation	[92]
	UVR + dissolved organic matter (DOM) (fresh-/seawater)	Photocatalytic halogenation of DOM	Formation of organobromine/-iodine compounds	[93]
	Natural clay colloids (SPM) (1) pH < IEP (2) pH > IEP	(1) Heteroaggregation (attractive electrostatic forces) (2) Weak affinity between NPs—SPM (both negatively charged) Adsorption of macromolecules (1) at a low HA conc.: NP surface charge neutralisation; (2) at a high HA conc.: NP surface charge inversion	Enhanced (1) NP aggregation (2) NP stabilisation	[86]
	HA (NOM) (pH < IEP)	Adsorption of macromolecules (1) IS < CCC: Adsorption of macromolecules (electrosteric repulsion) (2) IS > CCC: EDL compression + NOM entanglement	Enhanced (1) NP aggregation (2) NP stabilisation	[94]
	HA (NOM) (pH ≈ IEP)	Adsorption of macromolecules (1) IS < CCC: Adsorption of macromolecules (electrosteric repulsion) (2) IS > CCC: EDL compression + NOM entanglement	Induced partial disaggregation	[94]
	HA, FA (NOM) (pH > IEP)	Adsorption of macromolecules (1) low NOM conc.: interparticle bridging; (2) high NOM conc.: repulsive steric interactions	Enhanced (1) NP stabilisation (2) NP aggregation	[83]
	NOM (various)	Adsorption of macromolecules (1) low NOM conc.: interparticle bridging; (2) high NOM conc.: repulsive steric interactions	(1) Flocculation (dependent on NOM type, sometimes salt addition required) (2) steric NP stabilisation	[63]
	NOM	Adsorption of macromolecules	Photosensitiser AND ROS quencher (dominant)	[85]
	NaCl (Seawater) + Algae	Adsorption NPs—microalgae (note: NPs—NPs)	Intensified heteroagglomeration with increase in IS (note: homo-agglomeration is not affected by IS)	[95]
	NaCl (Seawater) (IS > CCC)	Aggregation	Induced NP aggregation	[96]
	UVR, seawater	Release of dissolved trace metals and inorganic nutrients	Greater bioavailability, bioaccumulation	[97]
	Siderophore-producing organisms	Biomolecular chelation of Ti ⁴⁺	Bioaccumulation, induced NP solubility	[8]
	Presence of Cu	Transport vector for heavy metals, Cu ²⁺ absorption on TiO ₂ surface	Bioaccumulation of Cu	[98]
	Presence of Cd, As	Transport vector for heavy metals, Cd ²⁺ , AsO ₄ ^{3−} absorption on TiO ₂ surface	Bioaccumulation of Cd, As	[99]
	Aged TiO ₂ under UVR (in presence of Cd ²⁺)	Production of singlet oxygen (¹ O ₂)	Higher sensitivity of cells to Cd	[100]

In sunscreens, nano-TiO₂ can negatively affect other sunscreen constituents such as organic UV filters. That is, the toxicity of the sunscreen can increase due to the TiO₂-induced photodegradation of oxybenzone [87], avobenzone, and octyl methoxycinnamate [88], which are commonly used organic UV filters. Furthermore, the behaviour and (eco-)toxicity of nano-TiO₂ in the environment can also be affected by other sunscreen components. For example, the use of the C₁₀-C₃₀ alkyl acrylate cross-polymer can increase the mobility and, thus, the concentration of nano-TiO₂ in the environment [81]. Moreover, EtOH is commonly used in sunscreens to improve the compatibility and ductility of the formulation. However, EtOH dissolves the organic coating of nano-TiO₂, leaving the NPs rather unstable and vulnerable to subsequent photolysis of superjacent layers [62].

Research on SPW has primarily focused on the impact of pool water ingredients on the integrity of nano-TiO₂ coatings. For example, Virkutyte et al. [65] ascertained that chlorine degrades potassium cetyl phosphate (PCP), a conventional emulsifying agent in O/W formulations, thus releasing PO₄³⁻ ions. This can accelerate the deterioration of the Al(OH)₃ layer by promoting the formation of AlPO₄ precipitates. Similarly, many studies have demonstrated that exposure to SPW worsened the protective Al(OH)₃ coating on the nano-TiO₂, thereby increasing the photocatalytic activity and toxicity of nano-TiO₂ [12,65]. Besides changes in the surface chemistry, particles can also become more spherical and smaller when in contact with SPW [64]. This is in line with the finding that the dissolved form of Ti dominates in SPW [89], which suggests that the smaller, spherical forms represent a progressed state of TiO₂ transformation. Jeon et al. [30] found that TiO₂ is likely to accumulate in SPW even after a multi-stage treatment (filtration, UV irradiation, heating, and chlorination) process.

Even though more studies have examined the fate and behaviour of nano-TiO₂ in natural aquatic environments compared to synthetic aqueous environments, the evaluation of synergistic interactions between multiple environmental influencing factors in both milieus is insufficient. Only a handful of researchers have studied various interacting factors in natural aquatic environments at once, and their results contradict. For example, Li et al. [101] assessed the effect of numerous natural water properties on the NP stability and found that the IS, especially Ca²⁺ and Mg²⁺, and the pH were the most important governing factors. In contrast, Slomberg et al. [84] observed that the nano-TiO₂ stability in natural and synthetic lake water could not be compared even if the water has the same pH and ionic composition. This observation supports the general advice to, if possible, collect field samples instead of conducting laboratory studies as only field studies reflect the actual chemistry of the environment. In the case of Slomberg et al. [84], this refers to various combinations of NOM, suspended particulate matter (SPM), and micro-organisms that seem to have significantly affected the particle stability.

Besides the influence of NOM on the aggregation and agglomeration behaviour, NOM can also affect the photocatalytic behaviour of nano-TiO₂ by either quenching or sensitising the generation of ROS [85]. Furthermore, a recent study has reported that nano-TiO₂ can initiate the halogenation of dissolved organic matter (DOM) in fresh water and seawater, which results in the formation of organobromine and iodine compounds [93]. Previous studies have also revealed that TiO₂ can increase the bioaccumulation of other environmental toxicants by effectively operating as a transport vector for heavy metals such as cadmium (Cd) or arsenic (As) [99]. Therefore, adverse effects indirectly arising from the presence of nano-TiO₂ in the environment should also be considered in ecotoxicity studies.

In summary, the prediction of the behaviour and fate of nano-TiO₂ based on identified predominant transport and transformation processes is still inadequate. Figure 2 schematically depicts the environmental processes that have been identified in aqueous environments. Due to the variety of interactions that occur in a single matrix, it is not yet possible to determine a distinct behaviour and fate of nano-TiO₂ in one matrix, not to mention to transfer and apply the outcome to another environmental matrix. Consequently, to provide a full picture, particle and environmental characteristics should be examined

comprehensively. However, this requires advanced analytical approaches that allow the characterisation of nano-TiO₂ in complex matrices.

3. An Analytical Challenge

To date, existing analytical techniques have been inadequate for quantifying and disclosing the state of nano-TiO₂ in diverse environmental compartments in a single analysis. Therefore, the (simultaneous) use of two or more complementary techniques is recommended as it enables the characterisation of additional particle properties and the cross-validation of results [102]. Frequently used techniques to determine the PS include (1) microscopy techniques, such as transmission electron microscopy (TEM) and scanning electron microscopy (SEM); (2) light scattering techniques, such as dynamic light scattering (DLS), multi-angle light scattering (MALS), or nanoparticle tracking analysis (NTA); (3) SP-ICP-MS; and (4) separation techniques, such as size exclusion chromatography (SEC), hydrodynamic chromatography (HDC), or field-flow fractionation (FFF). In their critical review, Mozhayeva et al. [103] discussed the key considerations when coupling SP-ICP-MS with separation techniques. Additionally, the review points out recent instrument and method developments that are achieved by, for example, optimising operating parameters such as plasma power and sampling position. We refer the reader to the above review for discussions concerning general SP-ICP-MS challenges.

Information about the crystalline structure of nano-TiO₂ can be obtained by, for example, X-ray diffraction. Lastly, the particle mass concentration can be determined by, for example, inductively coupled plasma atomic emission spectroscopy (ICP-AES) or mass spectrometry (ICP-MS) and the number concentration by, for example, SP-ICP-MS, TEM, or SEM; the latter two are often coupled with energy dispersive x-ray spectroscopy (EDS) to confirm the chemical composition. Adam et al. [102] and Krause et al. [104] offer a detailed review of the advantages and disadvantages of various analytical techniques.

Over the past decade, SP-ICP-MS has steadily gained popularity and is currently the technique of choice as it is possible to simultaneously determine the PS and its distribution, elemental composition, and number concentration [105,106]. In particular, for NP investigations in aquatic environments, SP-ICP-MS has emerged as the leading technique as it requires minimal sample preparation compared to, for example, microscopy techniques with access to greater information. Therefore, this section focuses on (SP-)ICP-MS and provides a concise summary of the studies that attempted to detect nano-TiO₂ in diverse field (Table 3) and laboratory (Table 4) aquatic environments. To the best of the authors' knowledge, this is the first review of the different approaches of sample collection, pre-treatment and (SP-)ICP-MS parameters focusing on Ti and nano-TiO₂.

Table 3. Overview of TiO₂ sample analysis with (SP-)ICP-MS (field studies). Abbr.: Air Water Interface AWI, Backwash BW, Cellulose Acetate CA, Collision Cell Technology CCT, Deionized DI, Fluorinated Ethylene Propylene FEP, Kinetic Energy Discrimination KED, (High-density) Polyethylene (HD)PE, Polyethersulfone PES, Polypropylene PP, Polystyrene PS, Polytetrafluoroethylene PTFE, Quadrupole Quad, Sector Field SF, Tangential Flow Filtration TFF, Time Of Flight TOF, Time Resolved Analysis TRA, Ultrafiltration UF, Ultrapure Water UPW, Water Surface WS.

Matrix	Sample Collection				Pre-Treatment			Analysis								Reference
	Location	Period	Filtration	Transport, Storage, Time Until Tested	Acid Digestion	Microwave-Assisted Acid Digestion	Fusion	Technology	SP Mode	Multi-Element	Mentioned Interferences	Gas	Dwell Time (ms)	Measured Isotopes	TiO ₂ SDL (nm)	
Freshwater (lake)	WS, 1 m depth	12 mos.	Unfiltered	PE bottles, 7 °C, <16 mos.		HNO ₃ , HF, H ₂ O ₂ , HCl		Triple Quad (CCT), TOF	×	Al, Fe, Mn, Pb, V	⁴⁸ Ca	NH ₃ , He	3, 4		81	[107]
	AWI		0.8 µm CA membrane													
Freshwater (lake)	WS, 1 m depth	12 mos.	Unfiltered			HNO ₃ , HF, H ₂ O ₂ , HCl		Quad (TRA)	×	Al, V, Ga, Y, Nb, Eu, Ho, Er, Tm, Yb, Ta	⁴⁸ Ca		10	⁴⁷ Ti	130	[108]
Freshwater (river)			0.45 µm	PE bottles, immediately		HNO ₃ , HF, HCl		Quad (TRA)	×		⁴⁸ Ca	Ar, He, no gas	3, 5, 10	⁴⁷ Ti	128 rutile, 44 anatase	[109]
Freshwater (river)	WS			PE, glass bottles, 4 °C, <24 h				Quad	×		⁴⁸ Ca		3	⁴⁸ Ti	100	[110]
Freshwater (creek)	WS	Hourly, over 72 h		PP centrifuge tubes, 4 °C				Quad (TRA), SF	×	Al, Fe	⁴⁸ Ca, ³² S ¹⁶ O		3	⁴⁹ Ti	79 (SF = 42)	[111]
Freshwater (river)	10 cm depth	At least twice daily, 3–7 days	0.02 µm PP	HDPE bottles, refrigerated, + HNO ₃ , <24 h				Quad	×				0.1	⁴⁹ Ti	48	[112]
Freshwater (urban runoff)				HDPE bottles, 4 °C, <24 h	H ₂ O ₂ , HF, HNO ₃			Quad		Nb				⁴⁷ Ti, ⁹³ Nb		[113]
Saltwater (river), SPW	WS	Over 9 h	0.7 µm	Amber bottles, cooled, <7 days				Quad (TRA)	×				10		148 river, 173 SPW	[114]
Saltwater (ocean)	WS, 40 cm depth	3× in 24 h	TFF: >0.5 µm, 0.02 < x < 0.5 µm	HDPE bottles, 4 °C		HNO ₃ , HF, H ₂ O ₂		Quad		Zn, Al, Fe, V						[115]

Table 3. *Cont.*[illegible]

Due to the significant variety of environmental compartments, only a few environmental matrices, such as freshwater (river, lake), have been examined more than once. Furthermore, most studies do not evaluate temporal variations. However, as shown in Tables 3 and 4, there is a consensus on collecting samples directly from the water surface, within the top 1 metre of the water column, or both. Furthermore, all samples for the total Ti concentration analysis were generally filtered using a nylon or cellulose acetate (CA) membrane with pore sizes between 0.2 and 0.8 microns. In contrast, samples for the analysis in single particle (SP) mode were seldomly filtered. Although the analysis should ideally be run shortly after the sample collection, the period between collection and analysis ranges from hours to months. The samples were mostly collected in (HD)PE containers and cooled during transport and storage.

The analysis of the total Ti concentration requires a pre-treatment of the sample to ensure the complete dissolution of Ti-containing particles. This is most commonly accomplished by acid digestion or microwave-assisted acid digestion using hydrofluoric (HF) and nitric (HNO₃) acids (Tables 3 and 4). Recently, alternative digestion procedures have been sought to avoid the use of highly corrosive and extremely toxic substances such as HF. For example, Mudunkotuwa et al. [122] achieved Ti recoveries of >90% by optimising the microwave-assisted acid digestion method using concentrated sulfuric (H₂SO₄) and HNO₃ acid at a 2:1 volumetric ratio and a temperature of 210 °C holding for 45 min. However, Markus et al. [120] subsequently established that any acid digestion of TiO₂ without HF is incomplete and results in underestimations of the real Ti concentration. Another approach to attain the complete digestion of TiO₂ to Ti⁴⁺ is fusing TiO₂ with ammonium persulfate in a porcelain crucible. The fusion requires heating over an open flame (e.g., a Bunsen burner) and dissolving the reaction product in dilute HNO₃ [119].

Another challenge associated with the determination of Ti using ICP-MS is the substantial polyatomic spectral interference that can originate from both native components of the environmental media such as chlorine or calcium and the oxyacids used for particle digestion such as H₂SO₄. As summarised in Tables 3 and 4, previous studies have mainly considered and attempted to prevent isobaric interferences occurring for the most abundant isotope ⁴⁸Ti (73.98%) with ⁴⁸Ca (0.19%) or ³²S¹⁶O (95.04%) by measuring other stable Ti isotopes [123,124]. For example, the isotopes ⁴⁷Ti and ⁴⁹Ti with abundancies of 7.32% and 5.46% [123] were equally often considered in field studies. However, all stable Ti isotopes (^{46–50}Ti) can interfere with sulfur-based species that stem from the H₂SO₄ matrix, such as ³²S¹⁴N¹H or ³²S¹⁵N with ⁴⁷Ti [125].

Table 4. Overview of TiO₂ sample analysis with (SP-)ICP-MS (laboratory). Abbr.: Collision Cell Technology CCT, Deionized DI, Kinetic Energy Discrimination KED, Quadrupole Quad, Sector Field SF, Sun Lotion SL, Time Resolved Analysis TRA, Ultrapure Water UPW, Wastewater WW.

Matrix	Pre-Treatment		Analysis								Reference
	Acid Digestion	Microwave-Assisted Acid Digestion	Technology	SP-Mode	Multi-Element	Mentioned Interferences	Gas	Dwell Time (ms)	Measured Isotopes	TiO ₂ SDL (nm)	
UPW			Quad (TRA)	×				0.1			[126]
	H ₂ SO ₄ , HNO ₃		Quad (CCT)				Ar, He		^{46–50} Ti		[127]
			SF, tandem Quad	×		⁴⁸ Ca, ³² S ¹⁶ O, ³⁶ Ar ¹² C	O ₂ , He +NH ₃	3, 5	^{47–49} Ti, ⁴⁸ Ca, ⁶³ TiNH	23–47	[128]
	(a) H ₂ SO ₄	(b) H ₂ SO ₄	Quad (CCT)				He		⁴⁷ Ti		[129]
DI water			Quad (TRA)	×			Ar	10	^{47,49} Ti	91–95	[130]
SL dispersed in 1% Triton X-100			Quad (KED)	×	Zn		He	5	⁴⁸ Ti, ⁶⁴ Zn	25	[131]
			Quad	×		⁴⁸ Ca, ³² S ¹⁶ O		0.1	⁴⁸ Ti	27–29	[38]
synthetic WW, sludge		HCl, HNO ₃	Quad	×			Ar	150	⁴⁸ Ti		[132]

As shown in Tables 3 and 4, most studies were carried out using quadrupole-based ICP-MS instruments. The performance of quadrupole-based systems can be improved by using the collision/reaction cell technology (CCT). This technology enables the elimination of polyatomic spectral interferences by operating in either the collision mode using inert gases and kinetic energy discrimination (KED) or the reaction mode using highly reactive gases to remove ions other than the analyte ions [133]. Other evolving technologies are the double-focusing magnetic sector field (SF) and the time of flight (TOF) analyser technologies. When operating in SP mode, both technologies seem to reach lower PS detection limits (SDL) than the quadrupole technology due to a better mass resolution [111].

Several studies have focused on reducing the SDL of TiO_2 , which is relatively high due to the low mass fraction of Ti (60%) to TiO_2 and the distribution of the total mass over several isotopes [128]. This may be reduced by careful consideration of the sample matrix, instrument parameters, and isotope selection. For example, Lee et al. [130] observed that low background noise and high instrument sensitivity could lower the SDL, where, for instance, the background noise can be minimised by working in the CCT mode or by using shorter dwell times. Additionally, even though the instrument sensitivity is higher for more abundant isotopes, the SDL of a less abundant isotope may still be lower due to its lower background noise, which can be derived from less isobaric interferences. The foremost effect of the background noise can also be seen when comparing the SDL of field (Table 3) and laboratory (Table 4) studies as the lower background noise in laboratory studies results in improved (i.e., smaller) SDLs.

The SP-ICP-MS analysis enables the detection and sizing of individual NPs at environmentally relevant concentrations [133] and the distinction between dissolved (ionic) and particulate forms of TiO_2 [134]. In fact, SP-ICP-MS is the only technique that can detect a mixture and a wide range of PSs at environmental concentrations without pre-concentration [135]. The high sensitivity and the wide dynamic range provide high size resolution, allowing the instrument to accommodate the expected polydispersity of TiO_2 . However, the technology may not always lead to accurate results as the method is based on several assumptions, such as spherical particle shape, which are for the most part difficult to confirm [105]. For example, the assumptions that the elemental composition is known or that the elemental components are uniformly distributed throughout the particle are problematic as particles often undergo surface treatments or particle doping. However, some assumptions can be minimised or eliminated, for instance, using the CCT technology ensures an analysis free from polyatomic interferences [105], but the high matrix complexity and variability mean that challenges remain in both laboratory and field scenarios.

There are only a few studies that have explored the prospects of using (SP-)ICP-MS as a multi-element analysis. The primary objective of those studies is to distinguish between natural (NNP) and engineered nanoparticles (ENP) based on different elemental ratios. While NNPs may contain high concentrations of, for example, vanadium (V), niobium (Nb), aluminium (Al), or iron (Fe), ENPs contain none or only low amounts of these elements [108,118]. Even if ENPs are enclosed by Al-bearing coatings, they can be distinguished from NNPs based on the considerably higher abundance of Al in NNPs. Accordingly, NNPs result in lower Ti/Al ratios (0.1) compared to ENP (20–50) [108]. However, using elemental ratios to distinguish between NNPs and ENPs requires sufficiently low SDL as otherwise NNPs can be mistaken with ENPs [118]. Elemental ratios are mainly calculated based on the total metal content of a sample [113,115]. Only recently have Loosli et al. [118] and Azimzada et al. [136] succeeded in determining elemental ratios on an SP basis.

(SP-)ICP-MS has been shown to be capable of detecting and identifying nano- TiO_2 in various matrices. However, to achieve a complete characterisation of nano- TiO_2 , the following challenges, which have not been sufficiently addressed, need to be examined:

- *Reduction of polyatomic interferences* New approaches in pre-treatments should be developed that can sufficiently digest the TiO_2 sample without the use of acids that

generate polyatomic spectral overlaps or require heavy safety measures like HF. Further developments in CCT technology could also reduce spectral interferences.

- *Reduction of SDL* Solely Hadioui et al. [116] have reached SDL as low as 19–44 nm for TiO₂ in rainwater and 27 nm for TiO₂ in SPW (Table 3). A low SDL is vital for detecting and accurately differentiating between small particles and the dissolved form [109,128]. If the resolution is too low, statements about the dominant form (i.e., dissolved or particulate) are not conclusive. Furthermore, adequately low SDLs are a prerequisite for effectively using (SP-)ICP-MS as a multi-element analysis [118].
- *Distinction between NNPs and ENPs using multi-element analysis* The advanced development of the (SP-)ICP-MS technique is required to effectively distinguish between TiO₂ inputs from natural and anthropogenic sources in various matrices. A promising approach is the calculation of elemental ratios on an SP basis [118]. However, this technique is still in its infancy. Moreover, a unique fingerprint of TiO₂ ENPs or NNPs should be identified to conclusively distinguish between the two [107].
- *Evaluating the coating degradation using multi-element analysis* The multi-element analysis could also be used to examine the potential deterioration of the particle coating. For example, Yamanaka et al. [117] have shown that Al and Ti (matrix: sunscreen), as well as Zn and Ti (matrix: SPW), can quantitatively and simultaneously be analysed using SP-ICP-MS. They verified the outcome by comparing the concentration results of the multi-element SP-ICP-MS analysis with the total metal concentration of microwave-digested samples. Future studies should investigate the suitability of this multi-element analysis for observing variations in the elemental composition on an SP basis.

In summary, the use of SP-ICP-MS is increasing due to its promising research outcomes. However, the detection and the characterisation of nano-TiO₂ using SP-ICP-MS is not practical in every environmental setting. Furthermore, the required measurements to determine particle behaviour and fate in each environmental media would preclude a realistic approach, both in terms of time and resource cost. Therefore, advanced modelling studies may help to address the gaps in the analytical approaches.

4. Modelling as a Complementary Method to Analytics

Given the existing limitations of the analytical methods for measuring nano-TiO₂, modelling techniques have been employed to predict the concentrations of nano-TiO₂ in the environment using material flow analysis (MFA), environmental fate modelling (EFM), or multimedia modelling. However, like analytical methods, modelling approaches (MFA, EFM) have their shortcomings, which are discussed below.

MFA models aim to estimate nano-TiO₂ concentrations in the environment based on product release flows. Input data includes (1) the (global) production volume (PV); (2) the product category (PC) and its share (SPC); (3) the particle release (PR) rates often considered in a life cycle (LC) perspective (i.e., production, manufacturing, use, disposal); and (4) transfer coefficients (TC) to include mass flow within and between environmental compartments. Since MFA models depend on the accuracy of data that is scarce and mostly has a low spatial resolution, only broad estimates can be made. More advanced models treat all input parameters as probability distributions to account for data uncertainty and variability.

To further refine MFA models, a probabilistic dynamic MFA model has been developed that includes nano-TiO₂ input and release dynamics [137]. Based on this model, different scenarios have been explored, such as the ban of TiO₂ in cosmetics. The scenario outcome predicts a significant reduction in emission of the total nano-TiO₂ in surface waters, as there is almost no delay in the release and a high percentage of the affected product type compared to the total shares [138].

Since MFA models generally do not consider transformation and only scarcely examine transport processes [139,140], most modelling efforts focus on nano-TiO₂ EFM, which has evolved over the past decade. EFM describes the behaviour and fate of nano-TiO₂ in one or more environmental compartments. The underlying mechanisms can be, for

example, modelled using a mechanistic approach, that is, one based on physical and biochemical principles [141,142].

Multimedia models consider the release, transport, and fate of nano-TiO₂ in multiple environmental compartments, such as air, water, sediment, and soil. The objective is to give a comprehensive picture of the NP behaviour. However, most multimedia models assume that environmental compartments are well-mixed, in a steady state, or both and hence are limited in their spatial or temporal resolution or both [143]. Exceptions are the multimedia models *MendNano* [144] and *NanoFATE* [145] that both consider time-dependent effects, such as variations in particle release, seasonal weather trends, and long-term particle accumulation. However, both models are not spatially explicit. Sani-Kast et al. [146] have incorporated the spatial variability in water composition by considering different river sections, but the water chemistry within one section was assumed constant.

A literature search shows that, despite the considerable progress in model development, models have not been able to fully consider the following aspects:

- The differentiation between the form (e.g., single, aggregated, or agglomerated) of nano-TiO₂ at the time of entry into the environment. A few models attempt to consider the transformation state; however, they merely manage to distinguish between pristine, dissolved, transformed (only core material), matrix-embedded, and product-embedded [147] or consider only certain situations, such as an aggregated form for particles originating from WW [146].
- The impact of manufactured and natural coatings on the fate and behaviour of nano-TiO₂ [148].
- Heteroaggregation/-agglomeration processes, which are not explicitly expressed as a function of environmental (e.g., NOM, pH, IS) and nano-TiO₂ properties (e.g., PSD, shape, crystallinity, coating) but rather indirectly included as part of the attachment efficiency/factor description [144,146]. Recently, the theoretical background and different experimental approaches used to study heteroaggregation have been thoroughly reviewed to at least improve the accuracy of attachment efficiency values of ENPs in natural surface waters [149].
- Environmental and nano-TiO₂ properties have not been comprehensively ranked in terms of their relevancy in determining the behaviour in complex systems. Meesters et al. [150] attempted to identify the most important physicochemical properties affecting the environmental fate in their previously developed *SB4N* model [143]. However, available models have not yet been successful in explaining the complex systems' behaviours adequately due to an oversimplification of the modelling assumptions.

Overall, all modelling studies highlight the need for greater integration of the impact of environmental conditions on the NP's behaviour as a temporal and spatial variable [27]. They further conclude that a more comprehensive collaboration between modellers and experimentalists would improve the model's performance [27,148].

Table 5 provides an overview of recent modelling studies and summarises the considerations for model formulation. Dissolution was only listed as a transformation process if the model referred to the dissolution of the coating and not the core material. Furthermore, high spatial resolution was only acclaimed when data was not averaged over large regions such as countries or large river grids. The time variability was acknowledged as factored when, for example, time-dependent particle release or seasonal trends and not steady-state conditions were assumed.

It is known that a comprehensive RA requires information about the concentrations in the environment (exposure) and the effects (hazards) of nano-TiO₂ in real-world conditions. As MFA and EFM models help to determine exposure levels, an improvement in the model formulation would concurrently lead to better results in risk forecasting. However, thus far, existing models cannot overcome and resolve the substantial data uncertainties and the insufficient understanding of the behaviours of the nano-TiO₂ in realistic environments. Therefore, a model technique that can manage data limitations and is suitable for complex environmental systems needs to be introduced.

Table 5. Summary of models for predicting concentrations of TiO₂ in the environment. Abbr.: Environmental System Parameters ESP, Hydrodynamics HD, Life Cycle LC, Particle Numbers PN, Particle Properties PP, Particle Release PR, Product Type PT, Product Use PU, Production Volume PV, Share of Product Category SPC, Sludge Treated ST, Transfer Coefficients TC, Waste Incineration Plant WIP.

Model			Technique		System Specification							Fate Processes		Reference
MFA	EFM	Multimedia	Probabilistic Model	Mechanistic Model	Data Type; Source	Source of Nano-TiO ₂	TiO ₂ Removal, Sinks	Nanoparticle Characteristics	Media Characteristics	Environmental Compartments	Space and Time Considerations	Transport Processes	Transformation Processes	
Release model; distribution model based on [28]			×		PV, SPC, PR (dt), TC; experiments, expert opinion		Temporal (in-use stock)/final sinks (soil, landfill, sediment)			Air, water, soil, ST soil, sediment, technical compartments	Temporally resolved; spatially averaged (EU)			[137]
Based on [28]	Based on [151]	×	×		Single input source (steady state): STP effluent, derived from previous MFA + PPr, ESP, HD			PSD, Assumption: Aggregated form	SPM (type, conc., size), constant within one river section	Water, sediment	Water chemistry effects spatially resolved (Rhône River, France)	Sedimentation, resuspension, advection	Heteroaggregation	[146]
×			×		PV, PC, PR (LC), TC; experiments, assumptions	Various (e.g., cosmetics, plastics, paint, coating)	Soil, sediment	Distinction: Anatase/rutile		Air, water, soil, ST soil, sediment, technical compartments	Spatiotemporally averaged (Denmark)	Sedimentation		[140]
	×	×	×	×	PV, SPC, PR (LC), PPr, ESP; literature, models, experiments, DLVO variables	Various (e.g., cosmetics, electronics, coatings, paints)	Transport processes	Physicochemical properties (e.g., PSD)	E.g., PS, ζ, of natural particles in colloidal or particulate form	Air, water, soil, sediment	Spatiotemporally averaged	Sedimentation (incl. burial), deposition, resuspension, erosion, advection	Heteroaggregation	[143]
	×			Based on [142]	HD, PU, input scenarios: WW (treated/untreated), sludge run-off		WWTP	Distinction: free/unattached particles, homo- or heteroaggregates	SPM (conc.)	Water, sediment	Spatiotemporally averaged (Rhine River, Germany, Netherlands)	Sedimentation, resuspension, advection	Homo-/heteroaggregation	[152]
	×	×			HD, PR (dt) (LC), ESP (dt)			PS, distinction: free particles or small homoaggregates, heteroaggregates	Water chemistry, soil properties (e.g., pH)	Air, water, soil, ST soil, sediment	Temporally resolved, limitation: spatial resolution (San Francisco Bay, USA)	Sedimentation (incl. burial), deposition, resuspension, soil run-off/leaching, advection	Heteroaggregation	[145]

Chen et al. [153] and Adam et al. [102] proposed the use of Bayesian networks (BN) to evaluate the risks of nano-TiO₂ in the environment. This probabilistic graphical model enables multiple interconnected system variables to be incorporated and does not require experimental data or mechanistic formulations as, for example, expert elicitation can be used as a data source. However, BN has not yet been used to evaluate the interactions, effects, and risks of nano-TiO₂, but it has been used as a tool

- To forecast the ecological risks of silver (Ag) NP exposure in aquatic environments (FINE model). The model integrates modules describing particle behaviour, exposure potential, hazard, and risk and was developed using expert knowledge [154].
- To predict the hazard potential and biological effects of five ENMs within the framework of a human health RA. The developed BN uses data obtained from the literature and expert elicitations and includes selected physicochemical ENM properties, human exposure routes, and biological effects [155].
- To assess environmental multimedia distributions of ENMs (BN-nanoExpo) based on simulated data derived from a previously developed multimedia fate and transport model (MendNano) [156].

Coupling different approaches such as dynamic simulation models with probabilistic modelling techniques can help to address the uncertainty in a system while capturing and examining the dynamics of a system's behaviour. Besides, data generated by one model can be used as an input for another model to improve modelling capability. This applies to spatial probabilistic modelling, in which data obtained from a geographic information system and a probabilistic model (e.g., BN, regression analysis) can be coupled to predict the spatially explicit probability of nano-TiO₂ in an environmental compartment [157]. It also applies to an analytical method combined with a probabilistic modelling technique (e.g., BN), which could also improve the prediction capability and, thus, support the decision-making of whether additional actions are required.

5. Conclusions

In recent years, the worldwide production of TiO₂ in sunscreens has increased by approximately 30% [158]. Due to this upward trend and the concerns about possible nano-TiO₂ health effects, there is a need for a thorough ecological and human health RA that requires an estimate of the nano-TiO₂ concentration in the environment and a better understanding of the particle behaviour as a function of particle and matrix characteristics.

In this review, relevant experimental studies examining the fate and behaviour of nano-TiO₂ in sunscreen, SPW, and natural aquatic environments have been summarised. The findings show that there are three key environmental factors, namely (1) pH and IEP; (2) IS and ion type; and (3) type and concentration of NOM that seem to significantly govern the particle behaviour in aqueous environments. However, due to the limited ability of existing analytical techniques to determine and characterise nano-TiO₂ in diverse media, the behaviour and fate of nano-TiO₂ are relatively unknown.

The impacts of physicochemical particle properties (e.g., PS, shape, crystalline phase, core composition, and surface chemistry) on the fate and ecotoxicity of nano-TiO₂ have also been reviewed. As the surface chemistry is one of the main determinants of the fate and ecotoxicity of nano-TiO₂, the paper has especially focused on studies investigating the particle coating's durability in diverse environmental conditions and has reviewed advances in surface treatments. The results reveal that, although numerous novel coatings have been introduced in the past three years, the suitability of existing and innovative coatings in resisting harsh environmental conditions has not yet been adequately examined.

(SP-)ICP-MS is known to be one of the most promising analytical methods to detect, quantify, and characterise nano-TiO₂ in environmental samples [134,159]. Therefore, this paper has attempted to critically examine the methodologies and results of laboratory and field (SP-)ICP-MS analysis. The results show that providing explicit and reliable test instructions to assess nano-TiO₂ in different matrices is challenging due to the absence of relevant studies and the considerable variability in the experimental procedure. Con-

sequently, more research is needed to investigate the actual behaviour of nano-TiO₂ in real-world conditions instead of in controlled laboratory environments. Nevertheless, the findings of this review paper are a starting point for researchers to accelerate the process of developing new methods to identify and detect nano-TiO₂ in complex media or to distinguish between ENPs and NNPs.

This review has found that even a high-resolution technique such as (SP-)ICP-MS is not adequate for the determination of NP characteristics required to measure nano-TiO₂ concentrations in the environment. Modelling studies (MFA, EFM) have evolved to compensate for the shortcomings of analytical techniques to estimate the concentration for RAs. The analysis of recent developments in modelling studies shows that, due to the complexity of the system and the difficulty in generalising the behaviour of various ENPs, most studies still exclude key processes such as surface transformation and lack spatial and temporal resolution. Therefore, additional modelling methods that consider interdependencies between variables and data-related uncertainties and are capable of handling a range of data from different sources are needed. In this respect, the probabilistic modelling tool BN has been proposed by some studies and appears to be a critical tool for future investigations.

In conclusion, relying on a standalone approach to predict nano-TiO₂ concentrations in the environment is not enough, not only due to shortcomings of the individual techniques but also due to the significant variety of interactions between particles and the environment. Therefore, a new approach combining the advantages of individual techniques while eliminating their shortcomings would strengthen the prediction abilities and produce results with speed and accuracy. This would be a critical advancement that is needed to design and develop new policies.

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