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MESOCOSM: a mesocosm database management system for environmental nanosafety

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Abstract

Engineered nanomaterials (ENMs) are intentionally designed and produced by humans to revolutionize the manufacturing sector, such as electronic goods, paints, tires, clothes, cosmetic products, and biomedicine. With the spread of these ENMs in our daily lives, scientific research have generated a huge amount of data related to their potential impacts on human and environment health. To date, these data are gathered in databases mainly focused on the (eco)toxicity and occupational exposure to ENMs. These databases are therefore not suitable to build well-informed environmental exposure scenarios covering the life cycle of ENMs. In this paper, we report the construction of one of the first centralized mesocosm database management system for environmental nanosafety (called MESOCOSM) containing experimental data collected from mesocosm experiments suited for understanding and quantifying both the environmental hazard and exposure. The database, which is publicly available through <https://aliayadi.github.io/MESOCOSM-database/>, contains 5200 entities covering tens of unique experiments investigating *Ag*, *CeO₂*, *CuO*, *TiO₂*-based ENMs as well as nano-enabled products. These entities are divided into different groups i.e. physicochemical properties of ENMs, environmental, exposure and hazard endpoints, and other general information about the mesocosm testing, resulting in more than forty parameters in the database. The MESOCOSM database is equipped with a powerful application, consisting of a graphical user interface (GUI), allowing users to manage and search data using complex queries without relying on programmers. MESOCOSM aims to predict and explain ENMs behavior and fate in different ecosystems as well as their potential impacts on the environment at different stages of the nanoproducts lifecycle. MESOCOSM is expected to benefit the nanosafety community by providing a continuous source of critical information and additional characterization factors for predicting ENMs interactions with the environment and their risks.

Keywords: Mesocosm testing, Database management system, Environmental exposure and hazards, Risk assessment, FAIR data.

2010 MSC: 00-01, 99-00

31 1. Introduction

32 A growing number of companies are manufacturing or using nanomaterials [1]. These engineered nano-
33 materials (ENMs) play an important role in the innovation of many industrial sectors such as construction
34 (self-cleaning concrete), cosmetics (sunscreens), textiles (antibacterial clothing), health (improving medical
35 imaging), paint (scratch resistant paint), etc. [2, 3]. However, the large specific surface area and the en-
36 hanced surface reactivities at the nanoscale have raised several questions these past 20 years regarding their
37 potential environmental risk (Exposure \times Hazard) if released in the Environment. Several groups around
38 the world have addressed this issue and generated data based on nanoecotoxicology approaches [1] focusing
39 on a single species or strain of model organisms. Such experiments are needed to gain knowledge on the
40 mechanisms and thresholds of toxicity (Hazard), but they separate the organism from their environment
41 (relevant Exposure) and community of organisms (i.e., the ecosystem), in which the environmental risks
42 of ENMs ultimately need to be understood. For a robust characterization of the environmental risk, the
43 complex ecosystem-level interplay between the organisms, their environment, and the ENMs needs to be
44 taken into account including but not limited to: aggregation state and sorption of (in)organic substances
45 [2, 3], oxidation-reduction potential, as well as ecological factors such as interacting organisms (e.g. microor-
46 ganisms, (in)vertebrates, plants, fungi), trophic levels present (e.g. primary producer, primary consumer,
47 secondary consumer) and trophic transfer potential [4, 5]. Particularly well-suited experimental devices
48 to engage such integrated and multidisciplinary approach are mesocosms [6, 7, 8]. In the scope of ENM
49 studies, mesocosms have been defined as indoor or outdoor experimental systems containing a portion of
50 the natural environment which is (i) self-sustaining once set up and acclimatizes without any additional
51 input of nutrients or resources, and (ii) that allows monitoring all (or the maximum of) input and output
52 parameters to draw a real-life mass balance [9].

53 For years, the SERENADE, for Safe(r) and Ecodesign Research and Education applied to NANomaterial
54 Development, consortium in collaboration with the Center for the Environmental Implications of Nan-
55 otechnology (CEINT) at Duke University, has been continuously conducting mesocosm testing to address
56 environmental nanosafety throughout the lifecycle of nanoproducts, from the early stages of production
57 to the end of life [10]. However, the experimental data produced were stored in non-standardized forms
58 limiting the accessibility, interoperability, and reusability of the generated data for further applications. To
59 meet this need, the development of a centralized mesocosm database management system for environmental
60 nanosafety that will allow to collect, standardize, and store all the exposure and hazard experimental data
61 obtained in mesocosms was required [5, 9].

62 Consequently, the mesocosm database management system for environmental nanosafety (MESOCOSM)
63 presented in this paper, will be one of the first free access database systems providing and managing ro-
64 bust environmental exposure and hazard data. The proposed system aims to achieve a highly organized
65 relational database along with an appropriate software application, consisting of a graphical user interface
66 (GUI), that facilitate processing and access to that data. The MESOCOSM database provides 5200 unique
67 experimental data on tens of unique mesocosm experiments based on *Ag*, *CeO₂*, *CuO*, *TiO₂*-based ENMs
68 as well as nano-enabled products [11, 12, 13] with different shape, size, surface coatings and matrix. These
69 data were collected from mesocosm testing to address environmental nanosafety throughout the lifecycle of
70 nanoproducts, from the early stages of production to the end of life. MESOCOSM will be an added-value
71 to model and forecast the behavior and fate of ENMs in the environment, as well as to assess their potential
72 environmental risks.

73 2. Overview of nanomaterial-related databases

74 Over the last decades, experimental studies on (eco)toxicologically, behavior and fate of ENMs have
75 significantly increased. This evolution comes along an increase in the number of databases (non-exhaustively
76 listed below), knowledge base [14, 15], web-based libraries [16], or also registry repositories [17, 18, 19] with
77 the financial support of the EU and US international organizations. An overview of ENM-related databases
78 is provided in Table 1.

79 Several of these databases are not specific to ENMs. Among others, the National Toxicology Program
80 database (NTP) contain modern toxicology and molecular biology data to identify substances (ENMs and
81 others) in the environment that may affect human health [20]. The ECETOC Aquatic Toxicity database
82 (EAT) is an ecotoxicological database regarding the toxicity of diverse substances to aquatic species in fresh
83 and saline waters [21]. The EAT database gives access to the Human Exposure Assessment Tools Database
84 (heatDB) which collects all publicly available sources of human exposure data. The National Institute for
85 Occupational Safety and Health database (NIOSH) provide databases focusing on occupational toxicology
86 information (ENMs and others) [22]. One last example, is the Ecotoxicological Risk Assessment database
87 (ERA) that includes the concentration ranges for various human-use drug residues, their potential effects
88 for aquatic organisms, and the temporal variations of the ecotoxicological risks [23].

89 Of course, with the enhanced research and development activities around Nanosciences and Nanotech-
90 nologies, ENM-specific databases were developed. Most of them focus on toxicity and/or ecotoxicity data.
91 For instance, the NanoE-Tox is a database on the nanoecotoxicity of eight ENMs that gathers data from
92 more than 220 scientific articles [24]. The Nano Environmental Health and Safety database (NanoEHS)
93 concerns the physico-chemical properties of ENMs, their biocompatibility and potential toxicity to human
94 health [25]. The NanoPUZZLES dataset gathers toxicity and cytotoxicity data. NanoEHS, NanoPUZZLES
95 are used to predict the relationships among the structure, properties, molecular interactions, and toxicity
96 of ENMs [26, 27]. The NanoMILE database aims to understand the mechanisms of ENMs interactions with
97 living systems and the environment [28]. Both NanoPUZZLES and NanoMILE used the ISA-TAB-Nano
98 template as an ENMs data exchange standard [29]. Other examples are the Nano Exposure and Contextual
99 Information database (NECID) that collects exposure measurements of nano objects and their agglomerates
100 and aggregates [30] in an occupational exposure perspective, or also the GUIDEnano database about the
101 human health risks of nano-enabled products all along the product life cycle [31]. Finally, one of the larger
102 European database is eNanoMapper that integrates generic nanosafety data from the scientific literature.
103 eNanoMapper includes functionalities for data protection and sharing, data quality assurance, and search
104 interfaces for different usages [32]. eNanoMapper is part of the computational infrastructure for toxicological
105 data management of ENMs.

106 Several of these ENM-databases are domain specific and are addressed to specific communities. For
107 instance, the NanoMiner database is designed for toxicogenomic researchers and contains more than 400
108 human transcriptome samples exposed to various types of ENMs [18]. The CaNanoLab database is intended
109 for the biomedical community who wants to use of nanotechnologies in biomedicine [33]. The NanoToxDB
110 database provides information to biologists on ENMs toxicity to a specific aquatic invertebrate, the *Daphnia*
111 *magna* [34]. The InterNano database is dedicated to the nanomanufacturing community [35]. It shares
112 standard nanomanufacturing processes and information on the properties of ENMs across sectors [36] to
113 facilitate the commercial development of nanotechnology.

114 Regarding the environmental exposure to ENMs, only two databases specifically address this domain: the
115 NanoInformatics Knowledge Commons database (NIKC) and the ECOTOXicology knowledgebase (ECO-
116 TOX). The NIKC, developed by the Center for Environmental Implications of NanoTechnology (CEINT),
117 provides a critical mass of experimental data generated in the CEINT center and related to environmental
118 exposure and hazard data. The ECOTOX is an open access repository including single chemical toxicity
119 data for aquatic life, terrestrial plants, and wildlife [37]. Developed by the Center for Computational Toxi-
120 cology and Exposure (CCTE) and the Great Lakes Toxicology Ecology Division (GLTED) which are both
121 components of the USEPA Office of Research and Development, the ECOTOX database incorporates three
122 independent databases of ecotoxicity data from various literature sources the ACQUIRE, PHYTOTOX, and
123 TERRETOX focusing on aquatic life, terrestrial plants, and terrestrial wildlife, respectively.

124 Finally, few of these databases act as networking tools as the NanoWerk Nanomaterial database which
125 provides information about nano conferences, nano events, nano companies, laboratories, and nanotechnol-
126 ogy applications [38], as well as the nanoHub database which provides information about available resources
127 (from video presentations to publications to simulation tools) [39].

128 Most of these databases were based on data extracted from published literature. Interestingly, few of
129 them combine the database with modeling tools to go further in the assessment and forecasting of the risks
130 for human and environmental health. As an example, the Nanomaterial-Biological Interactions Knowledge

131 Base (NBI Knowledge Base) is designed to interpret nanomaterial exposure effects in biological systems [40].
132 It acts as a depository for data but is also equipped with data mining tools to predict the biological inter-
133 actions of ENMs. The Online Chemical Modeling Environment database (OCHEM) provides experimental
134 measurements and properties associated to chemical compounds [41]. It also incorporates a modeling frame-
135 work to create a predictive model of biological and physicochemical properties of chemical compounds [42].
136 One last example is the Modeling Assays Platform for hazard ranking of engineered nanoparticles database
137 (MOD-ENP-TOX) and the Nanomaterials Experiment-based Predictor of Environmental Risk and Toxicity
138 (NanoExPert) database that contains information about nanoparticles properties and their interaction with
139 biological systems [23, 43, 44]. Both of them act as tools to predict the toxicity and ecotoxicity of ENMs.

140 This literature survey of the existing databases on ENMs highlights that most of them focused either on
141 the properties of ENMs, their hazards (toxicity, ecotoxicity, bioavailability) or the occupational exposure.
142 However, there is an obvious lack of databases about environmental exposure to ENMs. Gathering data
143 about the exposure and hazard of ENMs within ecosystems and taking into account different lifecycle stages
144 of ENMs-based products, the MESOCOSM database will fill this gap. MESOCOSM will be integrated with
145 the NIKC [50] and the eNanoMapper [32] databases. It will also be integrated into the search engine of the
146 international NanoInformaTIX database. NanoInformaTIX is a comprehensive database integrating several
147 relevant databases from EU/US projects supporting various aspects of ENMs nanosafety (materials, hazard,
148 environmental release, occupational exposure, omics, bio-nano interactions, pharmacokinetics, . . .), to im-
149 prove predictive (eco)toxicity assessment of ENMs during their whole life cycle. By itself, the development of
150 the MESOCOSM database will be an added-value in the field and its integration with other nano-database
151 will provide the needed tool for sustainable innovation pathways of nanotechnologies. In particular, the
152 quality of the data provided by the MESOCOSM database may support manufacturers and researchers to
153 consider the behavior of ENMs under different environmental conditions and during their entire life-cycle in
154 order to provide a complete view of their potential risks on the environment.

155 3. MESOCOSM database description

156 3.1. MESOCOSM database challenges

157 The database is available to all on GitHub repository. Scientists and industries can visualize the totality
158 or a part of the dataset, download the SQL database file and manipulate it with any database management
159 system (Oracle, Postgres, MySQL, DB2, . . .), remotely interact with the database via an application program
160 interface (API), or also download it with its application (graphical user interface) for local usage (on the
161 local computer or server).

162 As described in Figure 2, the application provides dialog boxes displayed on the frontend layer to in-
163 teract with users, allowing either (i) to notify the user that the input (insertion or modification) has been
164 successfully done, (ii) to confront the user with a choice, or also (iii) to ask the user to fill some missing
165 fields, and (iv) to ask the user to fulfill a request form or select search criteria to retrieve information or
166 refine the request, respectively. Through this graphical interface, users can interact with the MESOCOSM
167 database more flexibly and intuitively.

168 It is also expected that this application could encourage users to use the MESOCOSM database and
169 make it evolve. There are currently 5200 entities in the MESOCOSM database related to tens of unique
170 experiments investigating CeO_2 , CuO , TiO_2 -based ENMs, and nano-enabled products. But we hope that
171 with collaborative efforts, this number of entities could quickly evolve. Indeed, the database website invites
172 the large nanotechnology and nanoscience communities to submit additional data that could contribute to
173 the enrichment of the MESOCOSM database, as well as to address suggestions to improve the database.

174 The MESOCOSM database provides experimental data of interest to a wide range of users, including
175 manufacturers, researchers, and government agencies. It allows them to consult, update, export data on
176 environmental exposure to ENMs. With MESOCOSM, results obtained by international research groups can
177 be shared to the scientific community. This will encourage researchers to avoid repeating experiments that
178 have already been done, reject some research hypotheses and favor others. Only processed data, textual, and
179 already published are stored in the MESOCOSM database. Raw, non-numerical, unpublished data are not

Table 1: A summary of nanomaterial-related databases.

<i>Database</i>	<i>Ref.</i>	<i>Link</i>
NanoE-Tox	[24]	https://kbfi.ee/
ECOTOX	[37]	https://cfpub.epa.gov/ecotox/
NORMAN	[45]	https://www.norman-network.com/nds/ecotox/
DaNa	[14]	http://nanopartikel.info/
ERA	[23]	Not available.
EAT	[21]	http://www.ecetoc.org/
NIL	[16]	http://nanoparticlibrary.net/
NHECD	[46]	http://www.nhecd-fp7.eu/index.php?id=515
Nanomaterial Registry	[17]	http://www.nanomaterialregistry.org/
eNanoMapper	[32]	https://data.enanmapper.net/
nanoHub	[39]	https://nanohub.org/resources/databases
OCHEM	[41, 42]	https://ochem.eu/home/show.do
NECID	[30]	https://www.necid.eu/
NanoDataBank	[19]	http://nano.info.org/nanodatabank/
NanoMiner	[18]	https://ruoho.uta.fi/wp/estools/nanommune/index.php/
S2NANO	[47]	http://portal.s2nano.org/dataRepository/database.do
NIOSH	[22]	https://www.cdc.gov/niosh/chemicals/dbsandttools.html
MOD-ENP-TOX	[23, 43]	https://fys.kuleuven.be/apps/modenptox/
CaNanoLab	[33]	https://cananolab.nci.nih.gov/caNanoLab/#/
ModNanoTox	[48]	https://www.birmingham.ac.uk/generic/modnanotox/index.aspx
NBI Knowledge Base	[40]	http://nbi.oregonstate.edu/library.php
NanoMILE	[28]	https://ssl.biomax.de/nanomile/cgi/login_bioxm_portal.cgi
NanoExpert	[44]	https://nanoeexpert.usace.army.mil/#/Pages/ToolSelectionPage.xaml
NanoWerk	[38]	http://www.nanowerk.com/nanomaterial-database.php
InterNano	[35]	https://www.internano.org/user/login
NTP Database	[20]	https://tools.niehs.nih.gov/ntp_tox/
TOXNET	[49]	https://www.nlm.nih.gov/toxnet/index.html
GUIDEnano	[31]	https://tool.guidenano.eu/
NIKC	[50]	http://nikc.egr.duke.edu/#!/dataset
Nanodatabase	[51]	http://nanodb.dk/en/search-database
NanoToxdb	[34]	http://iittrindia.org/envis/Default.aspx
Nano EHS	[25]	http://icon.rice.edu/report.cfm
NanoPUZZLES	[26]	https://zenodo.org/record/35493#.Xv5g0EBuK_s

180 included in the database. Raw data collected from analytical instruments are manually refined, validated,
181 and organized before being stored in the MESOCOSM database.

182 The free access to the content of the MESOCOSM database and its integration into important databases
183 such as eNanoMapper, NanoInformaTIX, ... is expected to provide a vast collection of environmental
184 nanosafety data to support governments and regulators in developing legislation and recommendations
185 regarding the use of ENMs. Furthermore, in a safer-by-design perspective, using the MESOCOSM database,
186 manufacturers could better understand and assess the environmental exposure and toxic potential of ENMs
187 at each stage of their life cycle.

188 3.2. MESOCOSM database content

189 The MESOCOSM database contains all the information collected during the contamination of an ecosys-
190 tem by ENMs [3]. The simulation in the lab of this ecosystem is ensured by mesocosm testing, that offer
191 a means of providing meaningful environmental exposure and hazard data to inform about environmental
192 risk [11]. As described in Figure 1, this meaningful data can be divided into six groups:

- 193 • *The mesocosm testing information:* this group of information includes a general description of the
194 conditions and the design of the experiment, such as the Digital Object Identifier (DOI) of the publi-
195 cation in which the results of the experiment were published, the total duration of the experiment, the
196 type of ecosystem to be studied, the primary and secondary consumers, the benthic and planktonic
197 primary producers representing the food chain of the mimicked ecosystem.
- 198 • *The other additional information:* This group of information represents more general information on
199 the peer-reviewed publications associated with the data, such as details about the publication in which
200 the results of the experiment were published, details about the authors of the publication, usually those
201 who conducted the experiment, and details about the institutions to which the authors belong.
- 202 • *The physicochemical properties:* This set of parameters provides details of the physical and chemical
203 properties of the nanoparticle used as a contaminant. This group of parameters can include the chem-
204 ical nature, mineralogy, shape, coating, and initial size of the nanoparticle. This group also includes
205 the name of the contaminant which is specified by concatenating its physicochemical properties, e.g.
206 "Ag_Sphere_Citrate_20" corresponds to a silver (Ag), spherical, citrate-coated ENM with a size of 20
207 nm. Another item included is the sampling time representing the time for collecting the values from
208 samples to determine the experimental parameters [10].
- 209 • *The environmental end-points:* This set of parameters includes indicators for assessing the state of the
210 environment as function of time, such as the pH, temperature, conductivity, dissolved oxygen, total
211 organic carbon (TOC), oxidation-reduction potential (ORP) in the water column, surficial sediment,
212 and at the sediment-water interface, and the number of suspended particles in the water column.
- 213 • *The exposure end-points:* this set includes specific parameters used to measure and estimate the
214 exposure of the studied environment to metal-based ENMs as function of time, such as the total
215 concentration of metal in the surficial sediment, and water column, dissolved concentration of metal in
216 the water column, ENMs size in the column water, total concentration of metal in layings, juveniles,
217 adults, and digestive glands of adults, as well as the speciation in the water, sediment, layings, juveniles,
218 adults, and digestive gland.
- 219 • *The hazard end-points:* This group of parameters includes biomarkers to measure observable changes
220 indicating the hazard (acute or chronic) of ENMs towards living organism, such as the number of adult
221 and juveniles organisms, number of picoplankton and picobenthos, number of algae in the water col-
222 umn and surficial sediment, thiobarbituric acid reactive substances (TBARS) or the total antioxidant
223 capacity (TAOC).

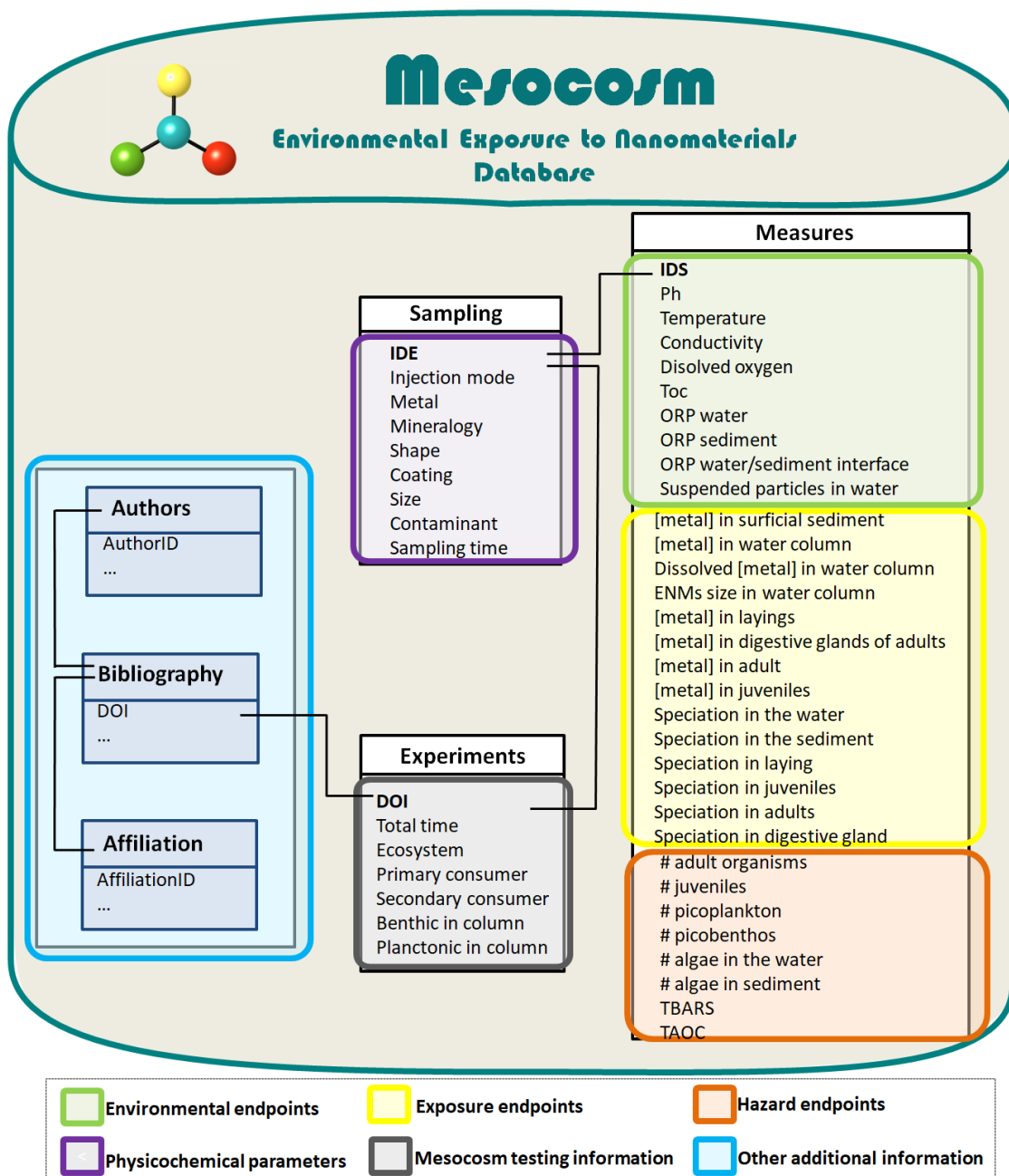


Figure 1: The MESOCOSM database management system content.

224 3.3. MESOCOSM database development

225 The MESOCOSM database system is implemented using JAVA programming language with MySQL. It
 226 has been developed into two levels, the back-end and the front-end layers. The back-end layer consists of the
 227 database server implementation, and the front-end layer consists of the graphical user interface. The back-
 228 end layer was firstly built on an Apache HTTP Server 2.4.4.1 with MySQL server. It was then hosted on
 229 an external server to be accessible to all users. The relational database was developed using the Structured
 230 Query Language (SQL) through the relational database management MySQL version 8.0. The interface

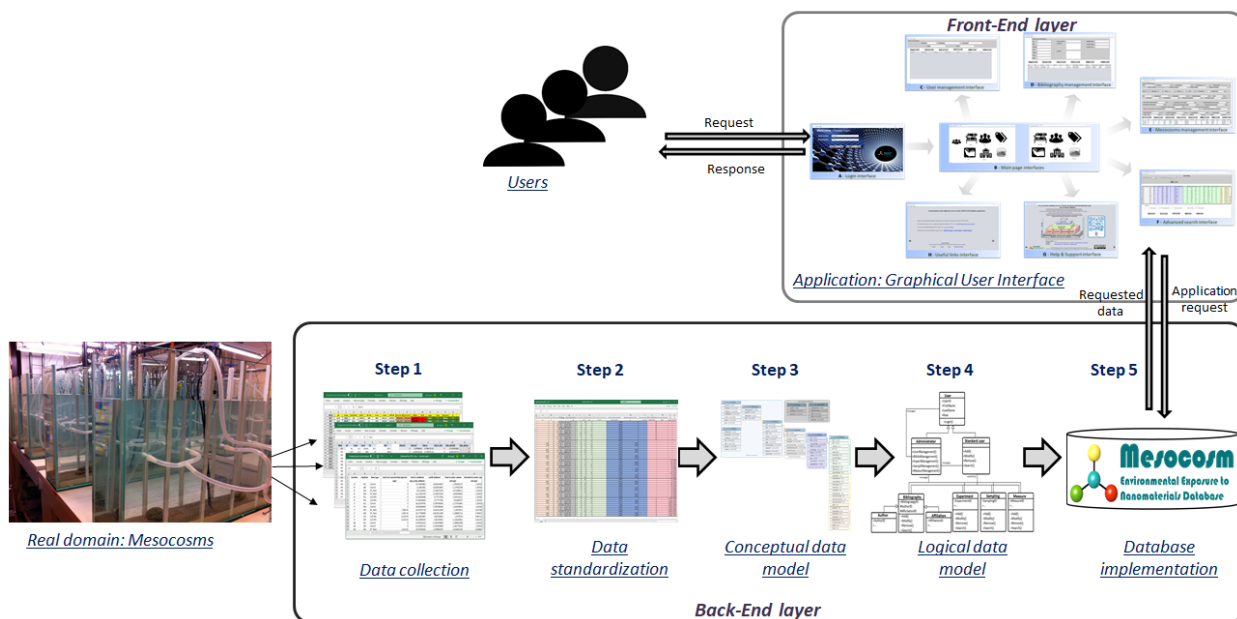


Figure 2: Methodology followed for designing and implementation of the MESOCOSM database management system.

231 component (front-end layer) is designed and implemented in JAVA programming language (Java SE 13.0.1).
 232 It allows users to access and manipulate data and services hosted by MESOCOSM database server. In
 233 addition, a web page has been developed especially for the MESOCOSM database system. This website
 234 provides a thorough description of MESOCOSM, its data, structure, some help documents, and links to
 235 download its user interface and its source files. This web page is implemented in HTML, CSS, JavaScript,
 236 and PHP languages, and is hosted on the GitHub repository.

237 The methodological steps followed during the implementation of the MESOCOSM database system are
 238 presented in Figure 2. In the following sections, each part of the methodology is described in detail.

239 **• Step 1: Data collection**

240 This first phase consists of collecting all the quantitative and qualitative data regarding the spatial
 241 and temporal behavior, fate and impact of ENMs obtained during mesocosm experiments. Raw data
 242 collected from analytical instruments are manually refined, validated, and organized. These data
 243 describe the exposure, the hazard, and the bio-physico-chemical properties of the ecosystems mimicked.
 244 All the files collected in this step contain data that are heterogeneous, not synchronized and collected
 245 from different individuals each one having its own style of structuring its information and its own
 246 domain of expertise.

247 **• Step 2: Data integrity and standardization**

248 Collected files were pre-processed to ensure their reliability, availability, maintainability, and efficiency.
 249 The experts propose a consistent data structure that is as general as possible without losing or affecting
 250 the quality of the data. This standard file prescribes the format that the team members must absolutely
 251 respect, and by which their collected information can be imported and stored in the MESOCOSM
 252 database. Accordingly, raw data collected from analytical instruments are manually processed and
 253 organized in this file before being stored in the MESOCOSM database. The standard file mainly
 254 focuses on the ENMs properties, environmental exposure and hazard endpoints.

255 **• Step 3: The conceptual data model**

As illustrated by Figure 3, the conceptual data model represents the schema of the database, i.e. the most important entities and their relationships. An entity is a real-world object, while a relationship is an association or a dependency between two entities. Based on entity-relationship diagrams, the objective of the conceptual model is to communicate contextual knowledge to any individuals who are unfamiliar to the domain. The conceptual data model presents also some detail about the entities such as their attributes (the properties that characterize an entity set), their cardinality (the relationships between tables), and their constraints (the conditions forced on the columns of the table to meet the data integrity).

• **Step 4: The logical data model**

As opposed to a conceptual data model, which may have very general terms, the logical data model includes a further level of detail, supporting both the architecture of the application and data requirements. It defines the primary keys, foreign keys, alternate keys, and inversion entities of the database. Table 2 presents the optimized logical data model of the MESOCOSM database which consists of nine tables. This logical data model uses indexes (primary keys) and foreign keys to represent data relationships, but these are defined in a generic database context independent of any specific database management system tool. For example, the user number (*userID*) represents the index of the *USERS* table and can uniquely identify a user. To distinguish foreign keys, a prefix consists of the sharp sign (#) is added to the beginning of the attribute(s) that represent(s) them. For example, the Digital Object Identifier (*DOI*) is the primary key of the *PUBLICATION* table and is also used as a foreign key in the *BIBLIOGRAPHY* table #*DOI* attribute to ensure the relationship between these two tables.

Table 2: The logical modeling of the MESOCOSM database management system.

<i>Table</i>	<i>Description</i>
1	Users (<i>userID</i> , <i>firstName</i> , <i>lastName</i> , <i>role</i> , <i>assignment</i>).
2	Bibliography (<i>bibliographyID</i> , # <i>authorID</i> , # <i>affiliationID</i> , # <i>DOI</i>).
3	Publication (<i>DOI</i> , <i>title</i> , <i>journal</i> , <i>year</i> , <i>volume</i> , <i>issue</i> , <i>page</i> , <i>contactAuthor</i> , <i>keywords</i> , <i>abstract</i> , <i>publishStatus</i>).
4	Author (<i>authorID</i> , <i>firstName</i> , <i>lastName</i> , <i>middleName</i> , <i>email</i> , <i>phone</i> , <i>web</i>).
5	Description (<i>descriptionID</i> , <i>tableDescription</i> , <i>field</i> , <i>note</i> , <i>dataType</i>).
6	Affiliation (<i>affiliationID</i> , <i>department</i> , <i>institution</i> <i>city</i> , <i>state</i> , <i>zipcode</i> , <i>country</i>).
7	Experiment (<i>experimentID</i> , # <i>DOI</i> , <i>totalDose</i> , <i>totalDuration</i> , <i>ecosystemType</i> , <i>injectionMode</i> , <i>primaryConsumer</i> , <i>secondaryConsumer</i> , <i>benthicInoculum</i> , <i>planktonicInoculum</i>).
8	Sampling (<i>samplingID</i> , # <i>experiment</i> , <i>metal</i> , <i>mineralogy</i> , <i>shape</i> , <i>coating</i> , <i>size</i> , <i>contaminant</i> , <i>samplingTime</i>).
9	Measure (<i>measureID</i> , # <i>sampling</i> , # <i>experiment</i> , <i>pH</i> , <i>temperature</i> , <i>conductivity</i> , <i>dissolvedOxygen</i> , <i>TOC</i> , <i>ORPwater</i> , <i>ORPsediment</i> , <i>ORPWaterSedimentInterface</i> , <i>numberOfParticlesInWater</i> , <i>ENMsSizeInWater</i> , <i>totalConcentrationOfMetalInSurficialSediment</i> , <i>totalConcentrationOfMetalInWaterColumn</i> , <i>dissolvedConcentrationOfMetalInWaterColumn</i> , <i>totalConcentrationOfMetalInWholeLayings</i> , <i>totalConcentrationOfMetalInTheDigestiveGland</i> , <i>totalConcentrationOfMetalInWholeAdult</i> , <i>totalConcentrationOfMetalInWholeJuveniles</i> , <i>changeInMetalSpeciationInTheDigestiveGland</i> , <i>changeInMetalSpeciationInLayings</i> , <i>changeInMetalSpeciationInJuveniles</i> , <i>numberOfAdultOrganisms</i> , <i>numberOfJuvenilesOrganisms</i> , <i>numberOfPicoplankton</i> , <i>numberOfPicobenthos</i> , <i>numberOfAlgaeInWater</i> , <i>numberOfAlgaeInSediment</i> , <i>TBARS</i> , <i>TAOC</i>).

• **Step 5: The database implementation**

The purpose of this step is to convert the logical model to a physical prototype. It consists in developing the programs to create the database and populate it. Once the database is implemented, numerous tests are performed to detect bugs or programming errors. This phase is expected to produce all the files that will be made available to the final user, including the programs, user manual and configuration files.

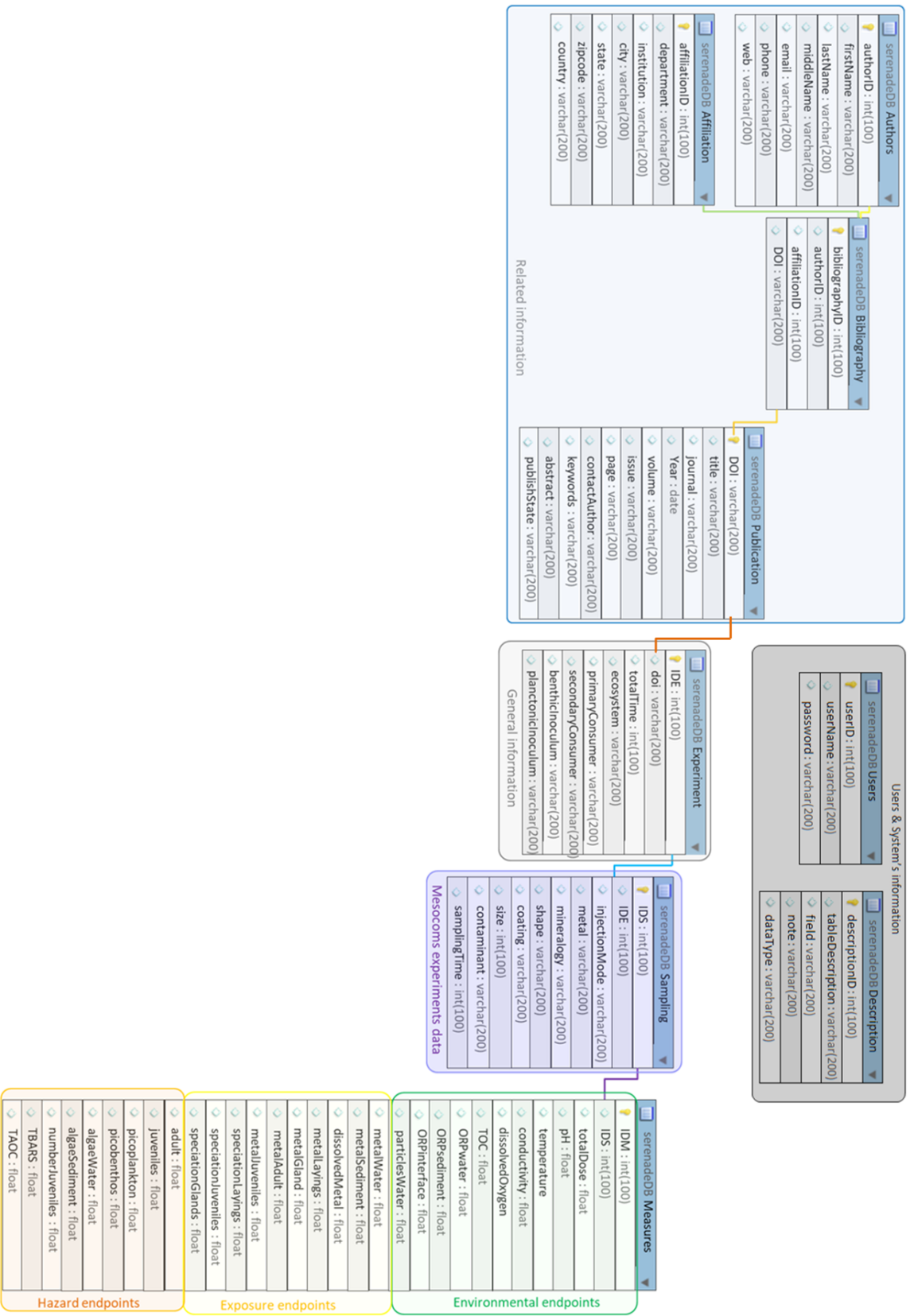


Figure 3: The conceptual data model of the MESOCOSM database system.

282 3.4. MESOCOSM database interface

283 The MESOCOSM user interface allows users to access and add new data in the MESOCOSM database
 284 system. This proposed interface provides a logical interface to the MESOCOSM database management
 285 system functionalities and specifies how users should interact with it. It has been developed as an open
 286 source JAVA library. Figure 4 presents the UML class diagram describing the architecture of our user
 287 interface by modeling its classes, attributes, methods, and relationships among the classes involved in our
 288 application. A class is represented by a rectangle separated into three parts (e.g. the *Users* class): (i)
 289 the first part contains the name of the class (e.g. "Users"), (ii) the second part contains the attributes of
 290 the class (e.g. "userID", "firstName", etc.), and (iii) the last part contains the methods of the class (e.g.
Log-in()).

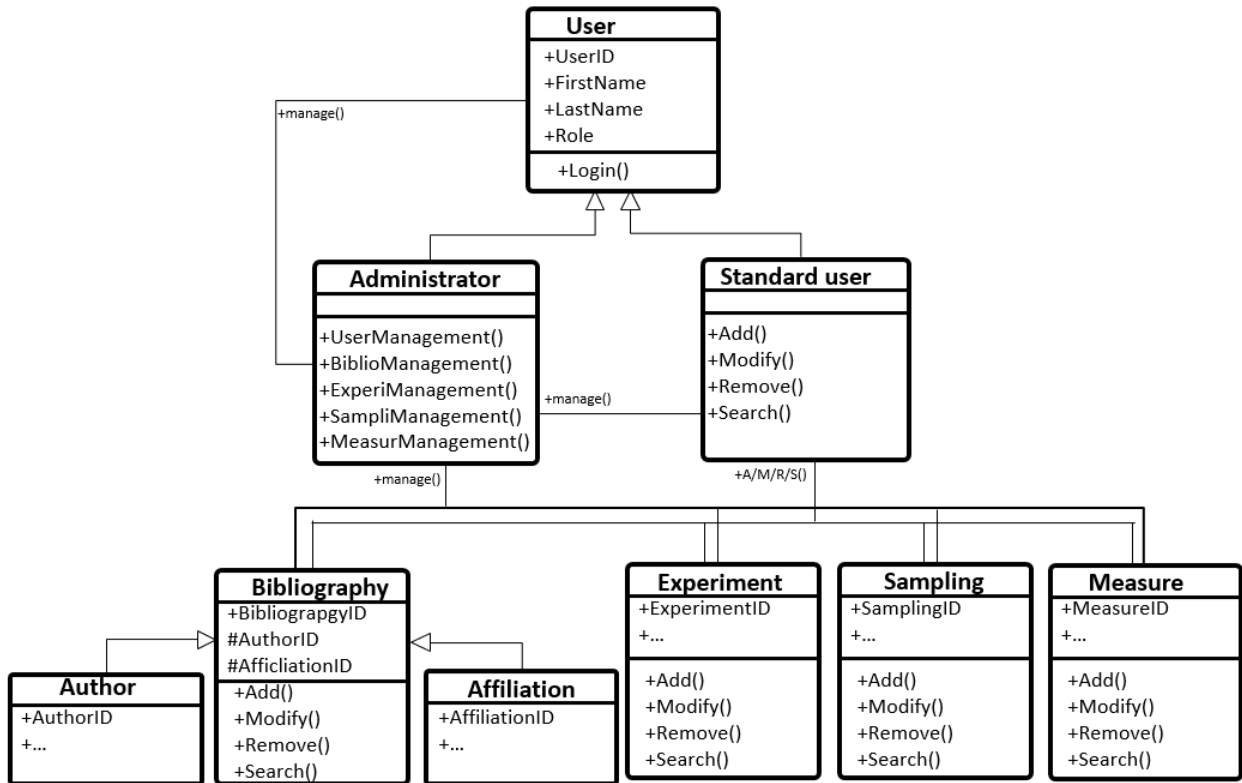


Figure 4: The class diagram representing the architecture of the proposed MESOCOSM database management system.

291 The main classes of our application are:
 292

- 293 • *Users* class contains all the users of the application.
- 294 • *Standard user* class includes all the activities handled by the internal user, such as Adding / Modifying
 295 / Removing / Searching bibliographies, publications, experiments, sampling, and measures.
- 296 • *Administrator* class includes all the methods supported by the administrator, such as manage users,
 297 bibliographies, publications, affiliations, authors, experiments, sampling, and measures.
- 298 • *Bibliography* class contains information on the peer-reviewed publications associated with the data
 299 (i.e. DOI, authors, and affiliation).

- *Sampling* class includes precise measurements on the experimental conditions of the mesocosm experiments (the sampling time, total duration of the experiment, type of ecosystem to be studied), and the physicochemical properties related to their contaminants (their size, surface, ...).
- *Measures* class contains the measurements related to the experiments such as the environmental, exposure and hazard endpoints.

The different classes forming our application are organized in two main packages, the *PackInterface* and *PackBase* packages. The *PackInterface* package contains all the classes dedicated to the *JavaX.swing* classes, and a class gathering the static methods of interaction among these classes (the display calls). The *PackBase* package includes the classes that manage the database connection, model the queries, define the objects of the model that can be modified by the application.

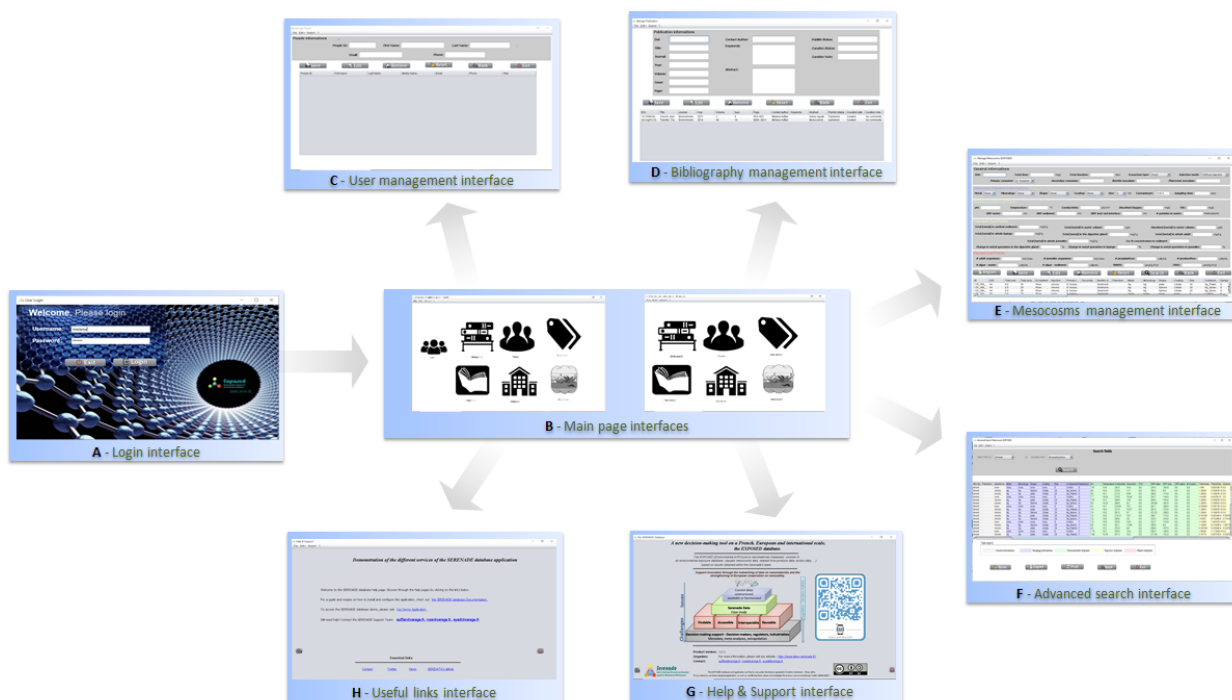


Figure 5: User interface of the MESOCOSM database management system. (A) The login page. (B) The home page: a specific home page for each user according to the user role. (C) The user account management page. (D) The bibliography management page. (E) The mesocosms management page. (F) The advanced search page. (G) The help & support page, and (H) The useful links page.

The MESOCOSM database management system is accessible via a user interface presented in Figure 5. Using this interface users can have access to the whole or part of the dataset depending on their needs. For instance, in their recent paper Nassar et al. [52] extracted from the database exposure and hazard data obtained in indoor aquatic mesocosms mimicking a pond ecosystem contaminated to CeO_2 ENMs. Applying multivariate analysis on these extracted data, they concluded that the exposure scenario constituted the main parameter to consider while investigating the risk for a given ecosystem. Following a single pulse dosing of CeO_2 ENMs, the global response of the pond ecosystem was time dependent, whereas a multiple dosing contamination failed to significantly perturb the system over a month. Interestingly, they highlighted that the ENMs surface coating played a secondary role and affect the global response of the pond ecosystem only in the short term only.

320 4. How fair is MESOCOSM ?

321 MESOCOSM was designed from the outset with maximum adherence to the FAIR principles that pro-
322 mote finding, accessing, interoperating, and reusing shared data [53]. From the beginning, the MESOCOSM
323 database system for environmental nanosafety was designed following the FAIR data vision to optimize
324 environmental exposure data sharing and reuse by humans and machines. The proposed database system
325 considers also the principles of linked data mentioned in the works of Bizer et al. [54, 55] demonstrating
326 that each entity must be correctly identified with a unique identifier, described in a semantic format, and
327 linked with other resources. The idea from the beginning was to identify all the records with a persistent
328 and unique identifier (PID) so that they can be located unambiguously by machines, and easily findable
329 by humans through the richness of the metadata used to describe them. Moreover, the database content is
330 registered and archived in different websites (the CEREGE website, GitHub repository¹, and Perma web
331 archiving service²) so that it can be easily found and accessible. Regardless of what may happen to the
332 original source, the archived record will always be available through the cited websites. Similarly, all datasets
333 have been published and are identified with unique DOI identifiers. To make the MESOCOSM database
334 content interoperable and FAIRness for machines, we have adopted a semantic format, the Resource De-
335 scription Framework (RDF). This semantic format is used directly as the primary medium for linked data in
336 MESOCOSM. Indeed, all the entities in the database are linked to other resources with permanent unique
337 URI identifiers through an ontology especially designed to support the development of the MESOCOSM
338 database system for environmental nanosafety. These identifiers can be considered unique across the World
339 Wide Web and therefore provide a solid basis for linking the MESOCOSM datasets. Indeed, each data
340 or entry in the database is associated with an ontological concept that defines its meaning. Indeed, each
341 data or entry in the database is associated with an ontological concept that defines its meaning so that the
342 datasets can be sufficiently understood by humans and can be reused appropriately. In addition, the RDF
343 format makes the MESOCOSM data accessible in the semantic web through the powerful SPARQL query
344 mechanism and rich metadata indexing. The reusability of the MESOCOSM database system is also ensured
345 by the use of an open source license. The default license of MESOCOSM is Creative Commons (CC-BY 4)
346 which allows users to download, modify and reuse the data without restriction, but attribution of the source
347 must accompany the reuse. The adoption of the four FAIR characteristics, makes MESOCOSM a modern
348 database making environmental exposure data valuable to a wide range of users, including manufacturers,
349 researchers, and government agencies.

350 5. Conclusion and perspectives

351 In this paper, we present MESOCOSM, a mesocosm database management system for environmental
352 nanosafety, developed to provide a collection of exposure and impact data to ENMs experimentally measured
353 using aquatic mesocosms. The database can be used in many different applications aiming to assess and
354 predict the ENMs behavior and fate in different ecosystems as well as their potential impacts on the envi-
355 ronment at different stages of the nanoproducts lifecycle. The data provided by MESOCOSM will actively
356 participate in optimizing the risk/benefit ratio over the entire life cycle of ENMs, from the manufacture of
357 an industrial product to its end of life, and, therefore support the "safer by design" approach which aims to
358 minimize the environmental exposure or hazards of ENMs.

359 Currently, all the entries stored in the MESOCOSM are published data obtained in mesocosms by the
360 SERENADE consortium. The MESOCOSM database will be frequently populated with new data obtained
361 in mesocosms facilities provided by groups working on nanosafety (as the CEINT center) but also, with
362 other literature data. Indeed, we are focusing on the exploration and use of text mining techniques for
363 enriching the MESOCOSM database. As such, we already proposed an ontology-based Natural Language
364 Processing (NLP) approach to automatically extract and transfer data from text sources (typically scientific

¹It offers provides hosting for software development and version control using Git command-line interface

²Perma.cc is a web archiving service for legal and academic citations created and maintained by the Harvard Law School Library

365 articles and expert reports) [56]. The proposed system, firstly, exploits the NLP techniques to intelligently
366 analyze textual documents and identify pertinent information from document [57], and secondly, uses a
367 domain ontology to semantically classify and categorize the extracted information according to its concepts,
368 thus associating the information with their corresponding attributes within the database. We demonstrated
369 how the automatic extraction system can extract environmental exposure to ENMs information from text
370 sources, classify them according to the ontology concepts, and automatically enrich the database. This will
371 significantly strengthen the MESOCOSM database by data coming from others groups using other mesocosm
372 designs.

373 Short-term perspectives would be the incorporation of additional user-friendly tools such as data analytics
374 tools based on some innovative algorithms for predicting the potential impact of ENMs on the environmental
375 on the long term or for categorizing the ENMs based on the potential risk for the environment.

376 Based on the relational model of the MESOCOSM database, an ontology is currently under develop-
377 ment. This ontology will provide the definition of vocabulary and specifies the meaning (semantics) of the
378 MESOCOSM database entries. The development of such ontology will improve the interconnectedness and
379 interoperability of the model, and therefore facilitate both the access and the interrogation of SERENADE
380 and CEINT datasets. In addition, the ontology will contribute to the extension of one of the most impor-
381 tant European nanosafety ontology, the eNanoMapper [32], to cover another major dimension of nanosafety:
382 Environmental Exposure.

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390 Conflicts of interest

391 The authors report no conflicts of interest.

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