Supplementary information

Literature collection. Primarily, literatures were searched from the search engines such as Google or Google scholar (https://www.google.com), Scopus (https://www.scopus.com), and Pubmed (https://www.ncbi.nlm.nih.gov/pubmed) with keywords 'daphnia', 'nano' and 'tox' to retain literatures related with *D.Magna* nanotoxicity studies. After initial search of literatures, more articles were further searched through references in initially searched literatures. Most of research articles were obtained through journals subscribed in Yonsei university library (https://library.yonsei.ac.kr) and Yonsei university medical library (https://ymlib.yonsei.ac.kr) or through the original text copy service of the libraries, and several research a rticles that were not available in the libraries were collected through ResearchGate (www.researchgate.net) or through direct link to PDF identified in Google search. To collect more information, supplementary information was collected together. Few research articles were unavailable unless payment was made for them; however, unavailable research articles contained toxicity data for silver, titatnium oxide or zinc oxide nanoparticles (NPs) which were already abundant NPs in the collected papers. Therefore, it was concluded that absence of few unavailable papers couldn't undermine the result of the analysis. Totally, 196 research articles were collected.

Filtering according to internal criteria. Among collected publications, research articles that didn't match the internal criteria were removed: (1) assay was not experimented according to OECD or US EPA TGs, (2) toxic response in the control media was higher than 20%, (3) toxic response in the control media was not given, (4) the number of *D.Magna* was not given, (5) different daphnia species were used in the assay, (6) coating material or chemicals treated with NPs caused toxic response by themselves without NPs, (7) descriptors for NPs were not provided, (8) The media treated with NPs contained more than two species including *D. Magna* except

algae, which is food for *D.Magna*, (9) phototoxicity assay results, (10) multigeneration assay results and (11) bioaccumulation or uptake assay results. It was assumed that experimental errors between assay results could be minimized by following protocols of OECD or US EPA test guidelines (TGs) (Standard 1). OECD and US EPA TGs mentioned that toxic responses in the control media shouldn't exceed 20%; therefore, the data in which the control data was not given or toxic responses were higher than 20% in the control media were considered unreliable and so removed (Standard 2 and 3). Each toxicity assays were conducted with different number of organisms. Even though concentration of NPs applied in the test media was equal, each *D.Magna* could be exposed to different concentration of NPs if the number of organisms in the test tube was different from one another; hence, literatures that mentioned the exact number of *D.Magna* in each test tube were collected (Standard 4). Due to the fact that we used broad terms for searching, some of literatures studied with different daphnia species. Such data was also removed because use of different species could contribute to increase of noise in data (Standard 5). Current study aimed to study toxic responses of NPs thus the data in which coating materials or co-treated compounds in the media caused toxic response by themselves without NPs were removed (Standard 6). In few research articles, TEM diameters on NPs were not provided. Since we can't be sure whether the experiments truly used NPs, data were removed (Standard 7). Concentration of NPs exposed to organisms could be influenced by the number of species in the media; hence, data experimented with more than two species including *D.Magna* were removed. However, algae was exception since it was food for *D.Magna* (Standard 8). Phototoxicity assays were focused on TiO_2 NPs alone; hence, it was impossible to assess phototoxicity of NPs with diverse core materials (Standard 9). Multigeneration assays aimed to check toxic response in offspring bred from an organism exposed to NPs. Such data were removed as toxic responses

were measured from *D.Magna* that was not directly exposed to NPs (Standard 10). Bioaccumulation or uptake assays were mainly conducted to check amount of NPs accumulated in an organism. It is related with toxic responses; however, it is not exactly toxic responses (Standard 11). 83 articles were remained after curating based on internal criteria[1-83] (Figure S1).

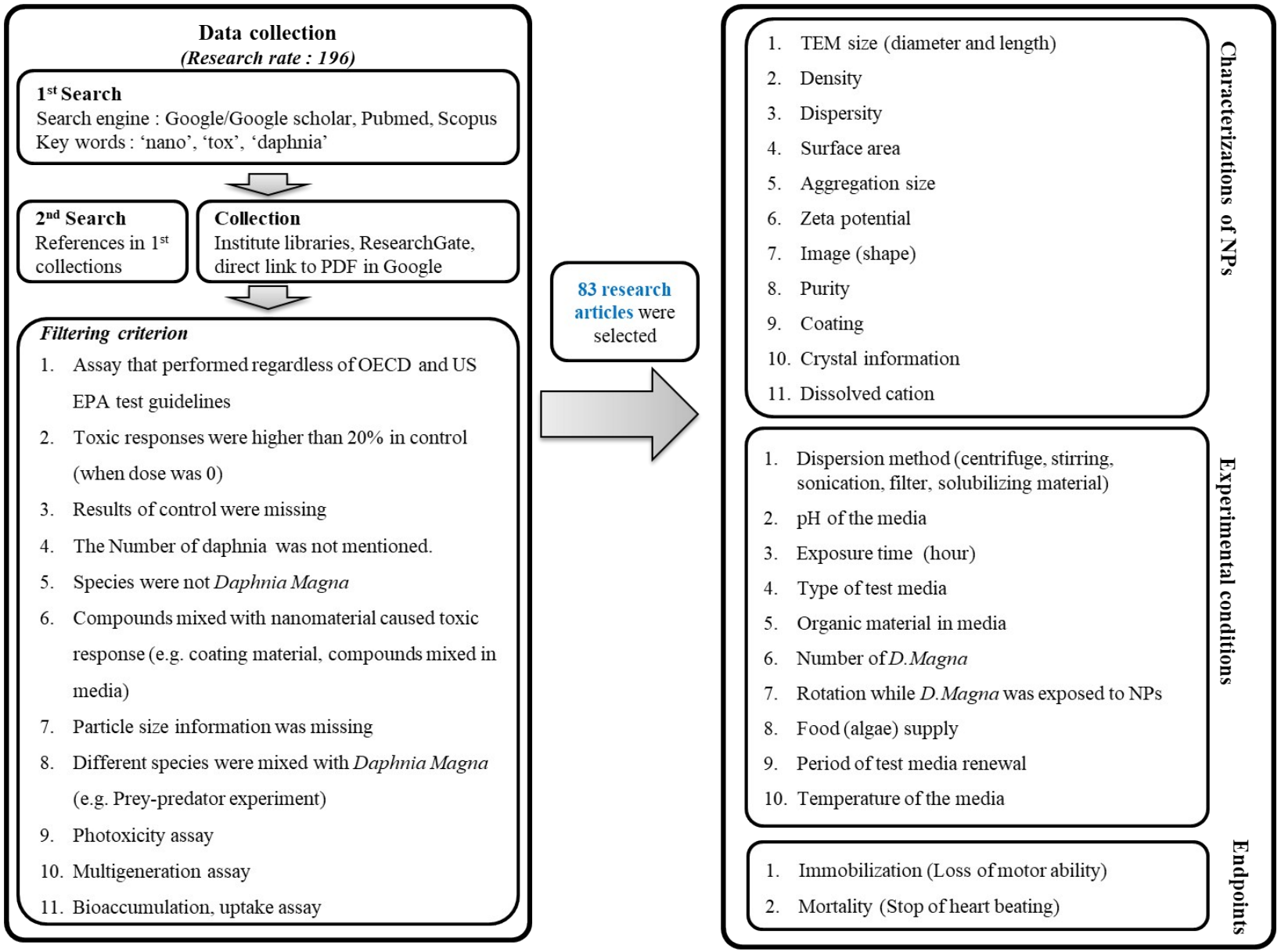

Figure S1. Process of data table preparation

Data sources

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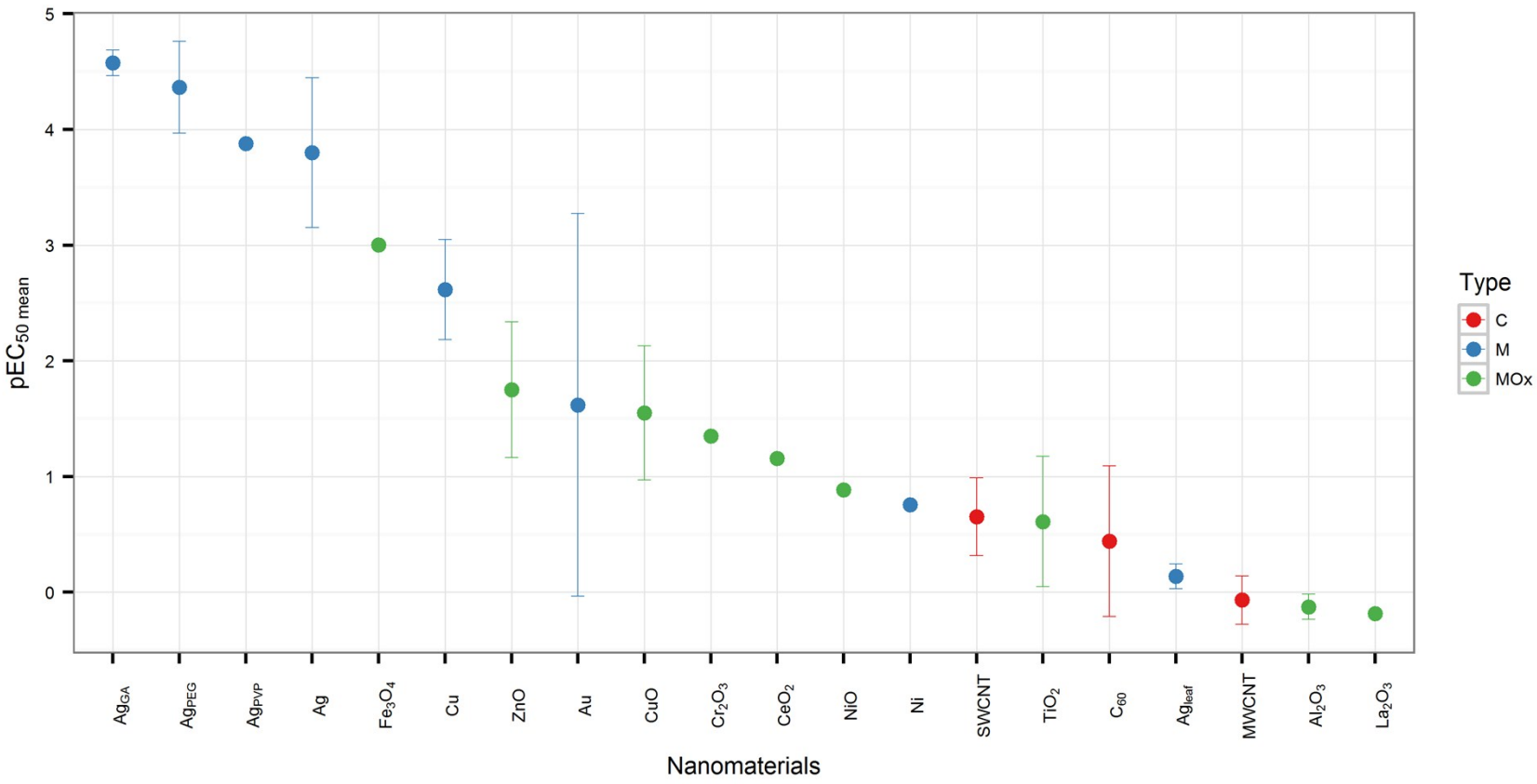
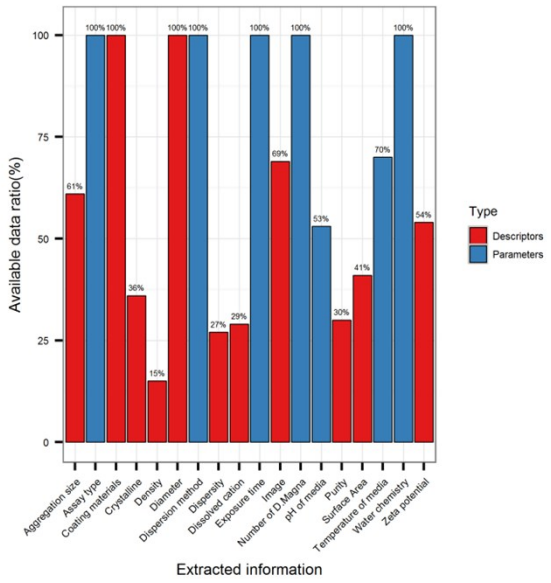


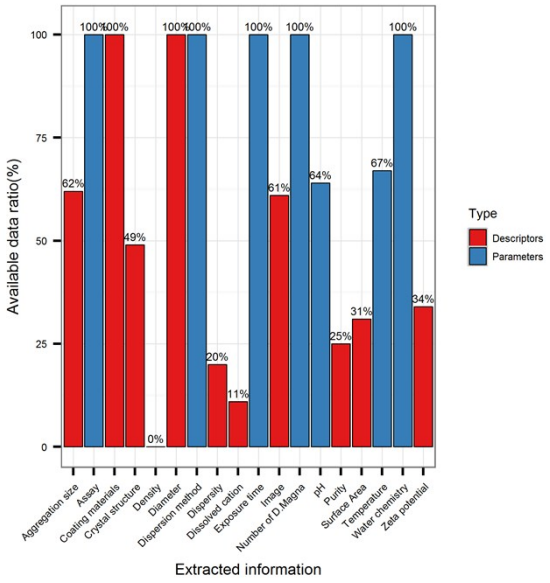
Figure S2. Nanomaterials were ranked according to the averaged pEC_{50}. It showed similar pattern with table 1 in which averaged pEC_{50} of NPs were listed regardless of exposure time.

Figure S3

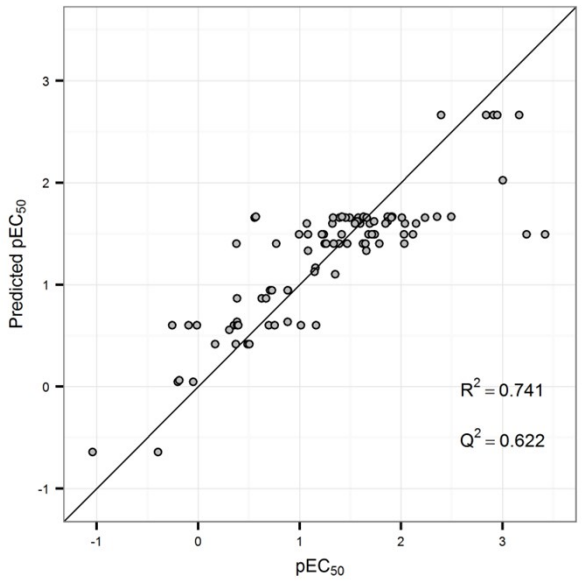
(A)



(B)



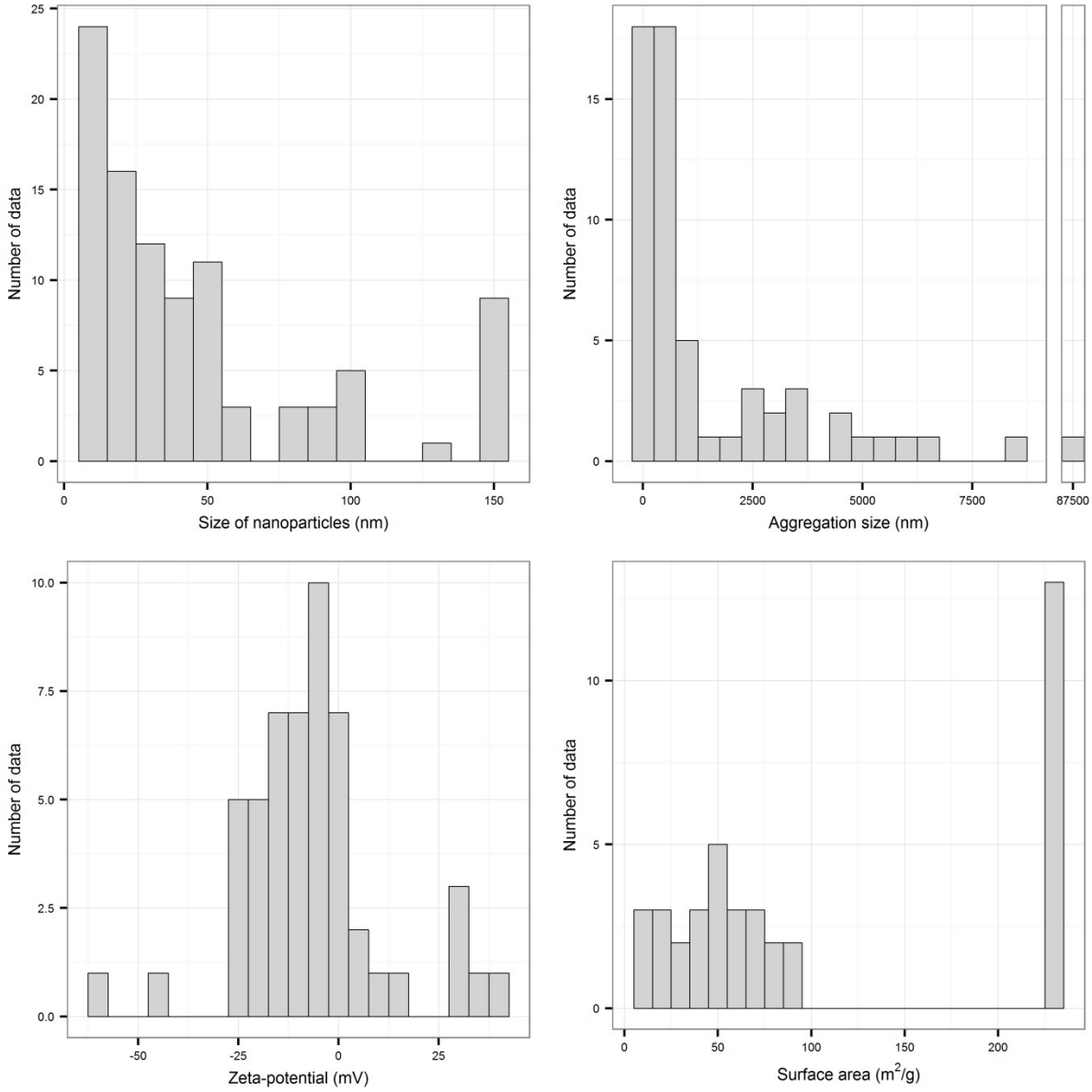
(C)



(D)

Pred \ Exp	TRUE	FALSE
TRUE	87	7
FALSE	15	196
Sensitivity	**Specificity**	**Accuracy**
85.29%	**96.55%**	**92.79%**

(E)


Number of data
Size of nanoparticles (nm)
Aggregation size (nm)
Zeta-potential (mV)
Surface area (m2/g)

(F)

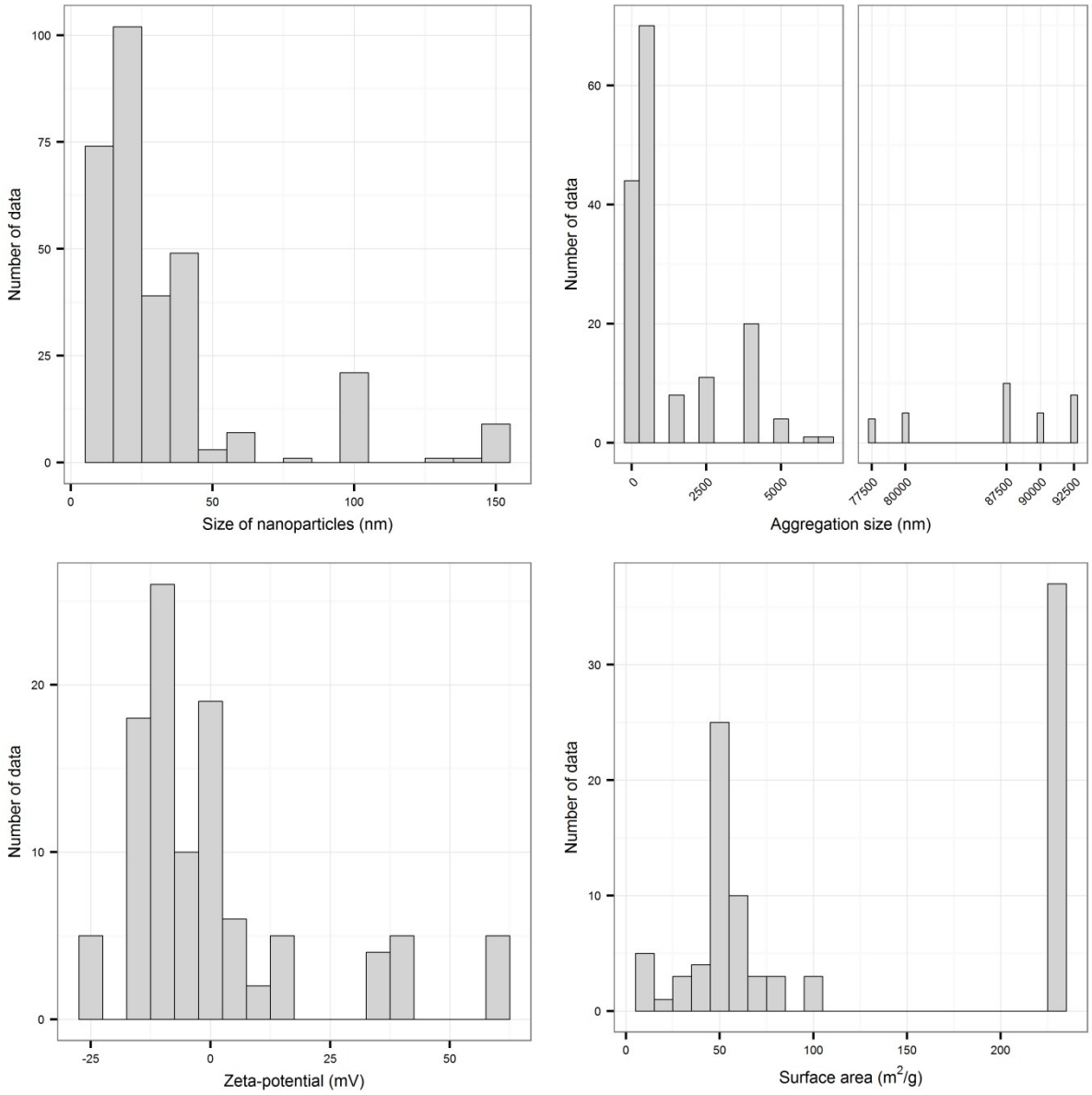
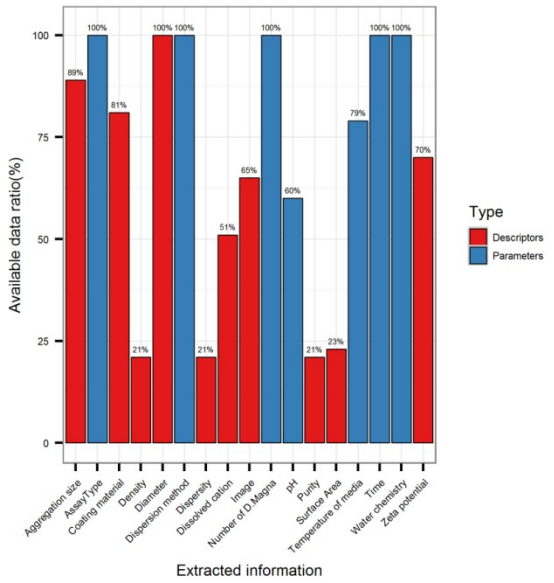


Figure S3. Available ratio of features was illustrated for pEC_{50} data (A) and for class data (B) in MOx class. Prediction values were compared with experimental values for the regression model (C), and performance of classification model was presented in confusion matrix (D). Distribution of TEM diameter, aggregation size, zeta potential and surface area of MOx NPs in pEC_{50} data (E) and class data (F).

Figure S4

(A)



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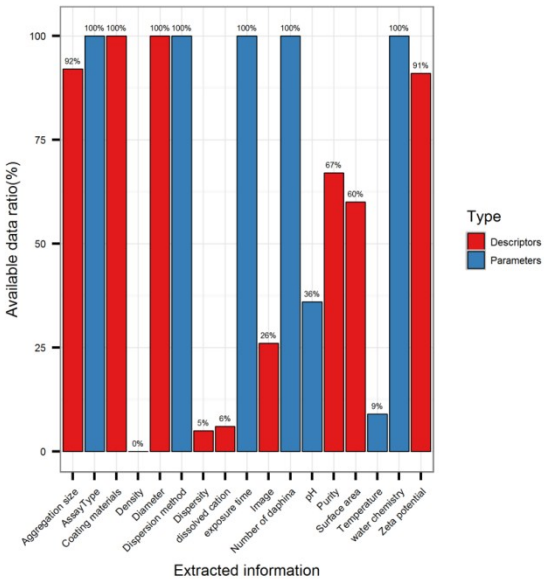
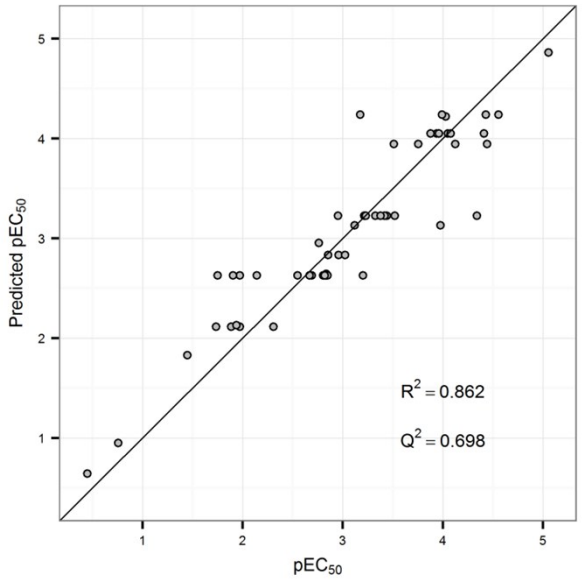
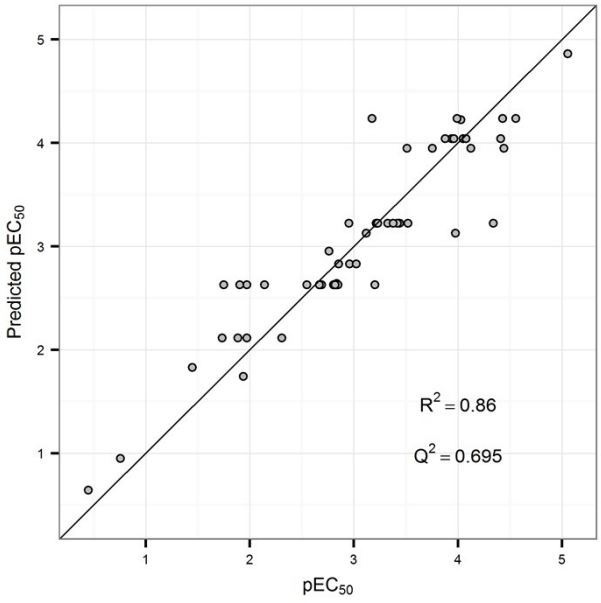


(C)



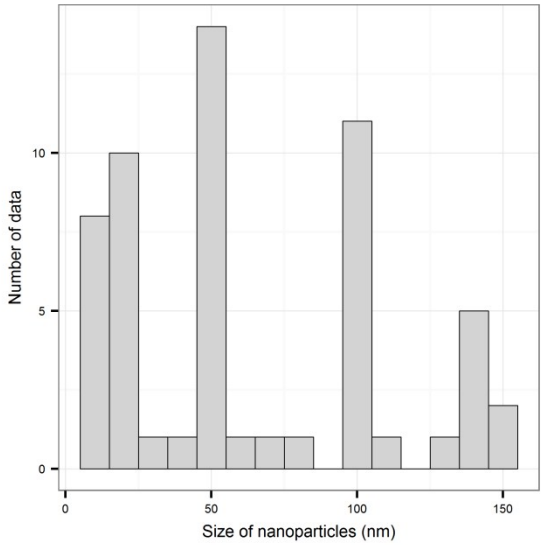
(D)

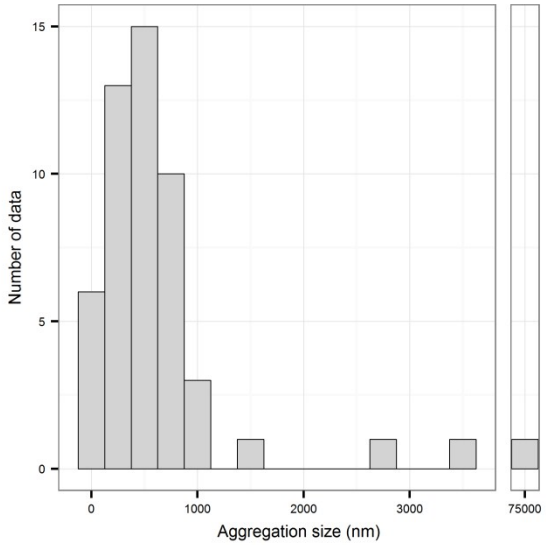


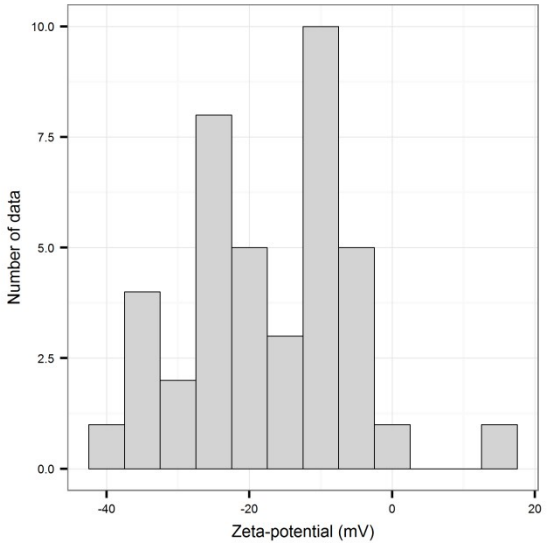
(E)

Pred \ Exp	TRUE	FALSE
TRUE	72	19
FALSE	0	151
Sensitivity	**Specificity**	**Accuracy**
100.0%	**88.82%**	**92.15%**

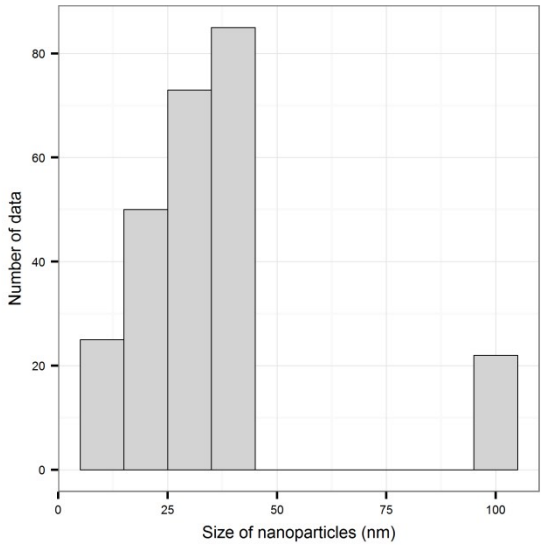
(F)

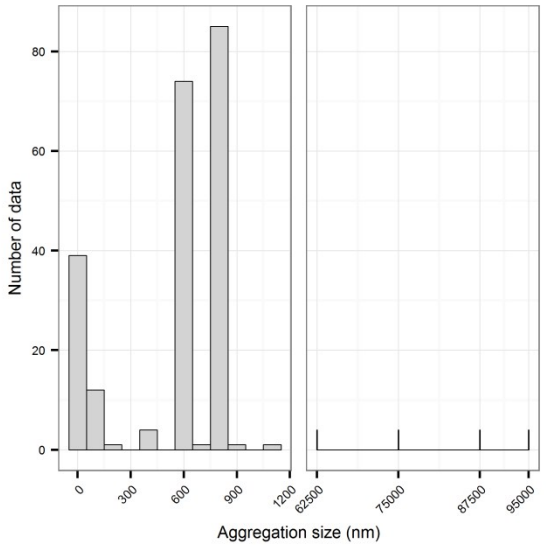

Number of data
Size of nanoparticles (nm)


Number of data
Aggregation size (nm)


Number of data
Zeta-potential (mV)

(G)


Number of data
Size of nanoparticles (nm)


Number of data
Aggregation size (nm)

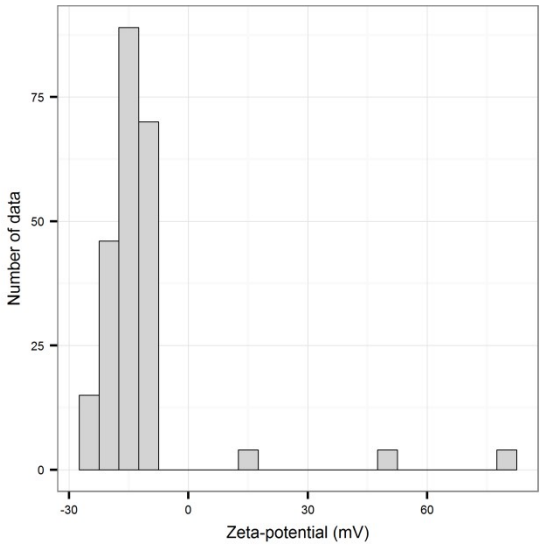
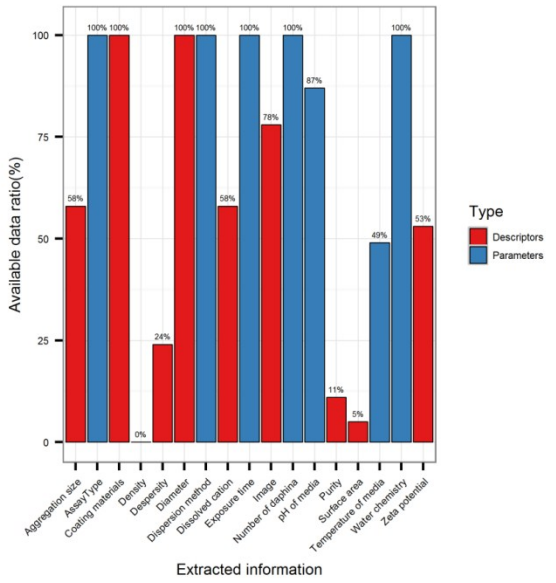

Number of data
Zeta-potential (mV)

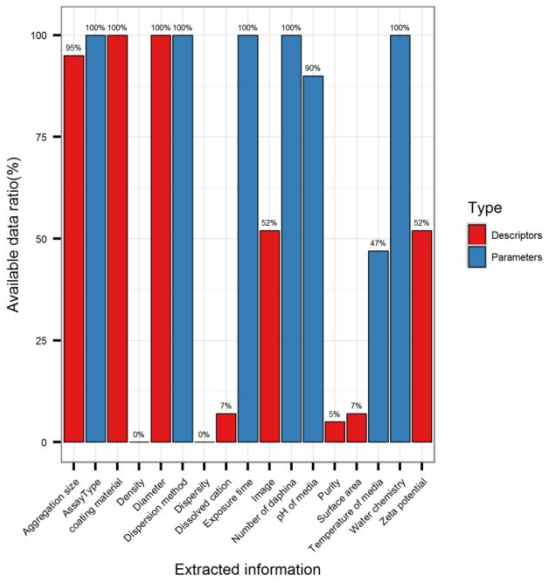
Figure S4. Available ratio of features was illustrated for pEC_{50} data (A) and for lass data (B) in M class. It was unusual that ratio of available aggregation size and zeta potential was significantly high. Prediction values were compared with experimental values for regression model when covalent index was selected first (C), and standard enthalpies of formation of gaseous metal atoms was selected first (D). Performance of classification model was presented in confusion matrix (E). Distribution of diameter, aggregation size and zeta potential for M NPs in pEC_{50} data (F) and class data (G) were plotted. Ratio of available surface area data was only 23% ($7 m^2/g$ of Cu NP and 2.24 m^2/g of Ag NP) for pEC_{50} data, and only three values (0.4, 2.24 and 2.4 m^2/g of Ag NPs) were available for class data.

Figure S5

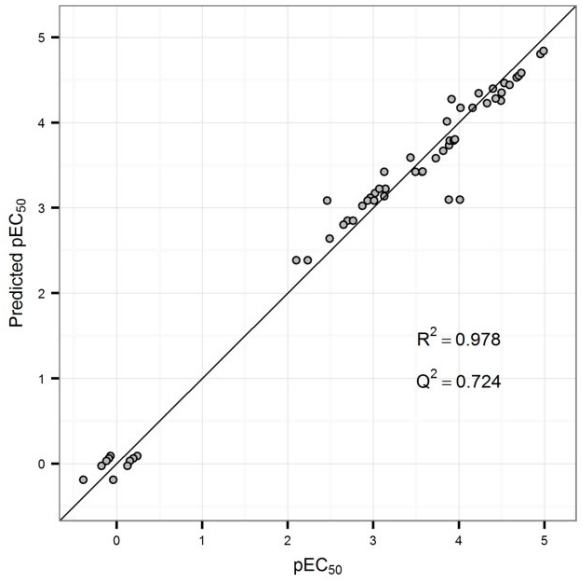
(A)



(B)



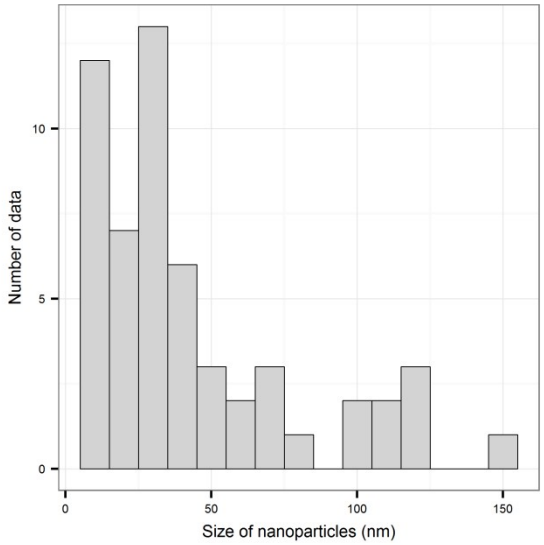
(C)

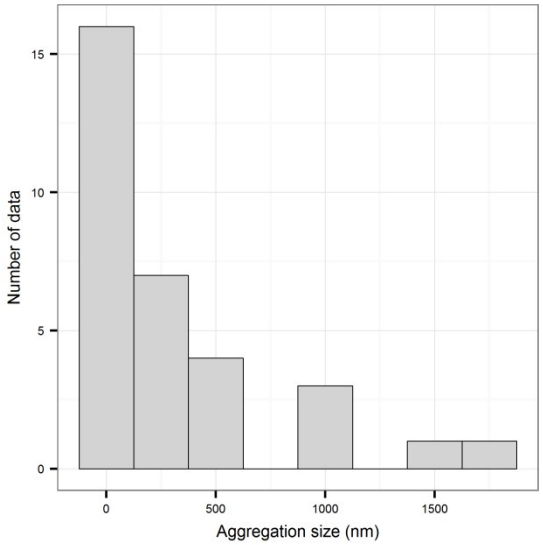


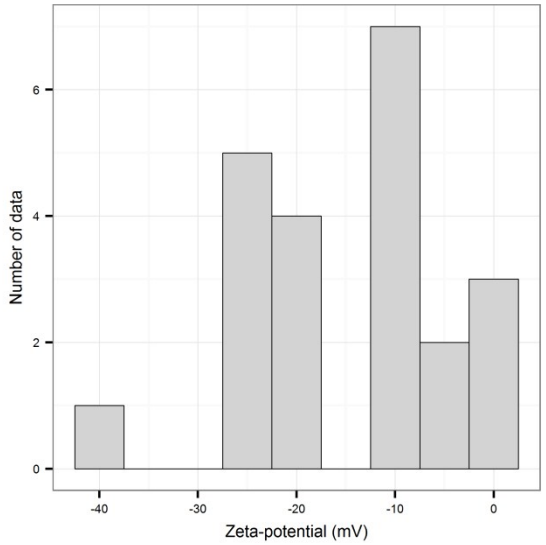
(D)

Pred \ Exp	TRUE	FALSE
TRUE	14	0
FALSE	6	40
Sensitivity	**Specificity**	**Accuracy**
70.00%	**100.0%**	**90.00%**

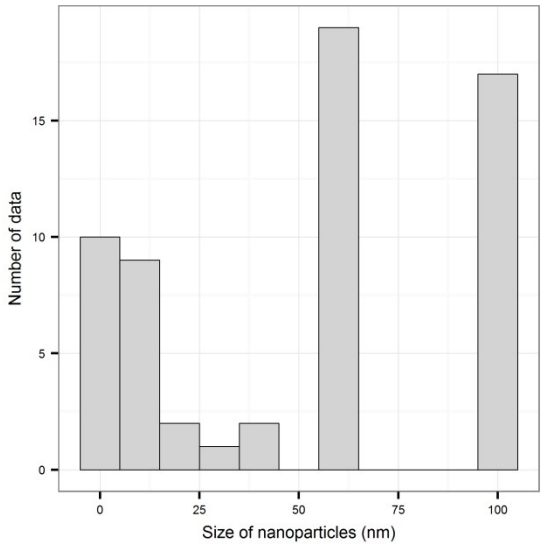
(E)

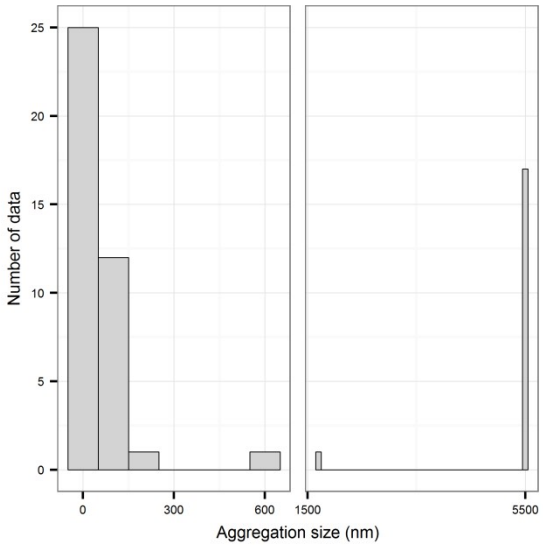

Number of data
Size of nanoparticles (nm)


Number of data
Aggregation size (nm)


Number of data
Zeta-potential (mV)

(F)


Number of data
Size of nanoparticles (nm)


Number of data
Aggregation size (nm)

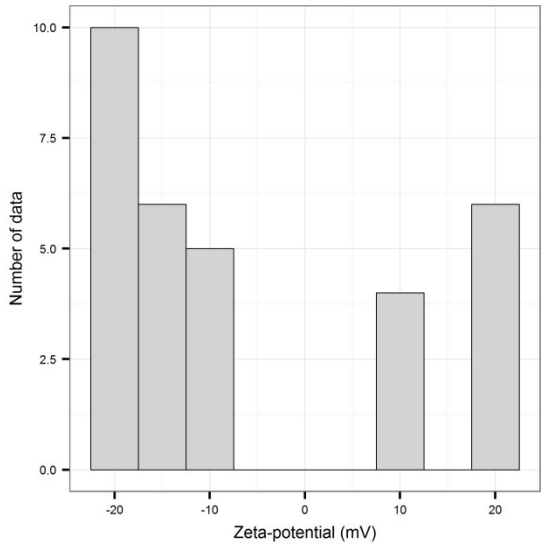

Number of data
Zeta-potential (mV)

Figure S5. Available ratio of features was illustrated for pEC_{50} data (A) and for class data (B) in coated M class. Prediction results compared with experimental values for regression model (C), and performance of classification model was presented in confusion matrix (D). Distribution of diameter, aggregation size and zeta potential for pEC_{50} data (E) and class data (F) were plotted. Ratio of available surface area data was only 5% and 7% (16.3m^2/g of citrate-coated Ag NP, 2.22 and 8.18m^2/g of extracts-coated Ag NPs) for pEC_{50} data and class data.

Case study: Carbon nanomaterials (CNMs)

Quantum mechanical (QM) descriptors were calculated from fullerenes. In toxicity assays where fullerenes were treated with organic molecules, their structures were used separately to calculate QM descriptors. In QM descriptor calculations, structure was optimized first using PM7 in MOPAC 2016, and then the descriptors were calculated.

For pEC_{50} data, only 12 data points were available with C60, C70, single-wall carbon nanotube, and multi-wall carbon nanotube (Figure S6A). For class data, 42 data points were obtained, and the dataset consisted of C60 and C70 (Figure S6B). Even though data size was small, authors believed that meta-analysis results on carbon nanomaterials are still valuable since it shows current data status on *D. Magna* toxicity study using carbon nanomaterials, and potentially significant features for describing toxic response of *D. Magna* to carbon nanomaterials.

The regression model achieved almost similar performance in R^2 and Q^2 (0.8) with exposure time (Time), application of filter (Filter), and shape score (Shape) (Figure S6C). The classification model achieved 72.70% accuracy, 80.10% specificity, and 64.80% sensitivity using exposure time (Time) and dipole moment of fullerene (Dipole) in bootstrapping (Figure S6D). Dipole moment of fullerenes was significant as it was related with the reactivity of fullerenes. Exposure time was more influential than concentration of fullerenes as most were aggregated in the media, while concentration contributed only to the size of aggregated deposits. An increase in concentration caused an increase in interaction between fullerenes as the distance between fullerenes became smaller at higher concentrations. Therefore, concentration did not contribute significantly to toxic responses to fullerenes. Dispersion methods were essential to develop prediction models in the above case studies; however, they were not used for the

fullerene model as the strong hydrophobicity of fullerenes may nullify the effect of dispersion methods.

In publications, few CNMs assay succeeded to observe toxic responses while majority failed to measure toxicity. According to the descriptions in the studies that failed to measure toxicity, common reason for the failure is aggregation of CNMs. It implied that CNMs' toxic responses were observed when CNMs were successfully dispersed in aquatic condition. In natural water environments, the water current is much more rapid and dynamic than that in experimental conditions. If CNMs can be dispersed in natural water systems, then they are potentially hazardous to aquatic organisms even though their toxicity was not measured in the assays due to aggregation. As dispersion methods applied in the assays did not closely represent real currents of natural water, it is necessary to design a dispersion protocol that can accurately represent water currents in nature.

Figure S6

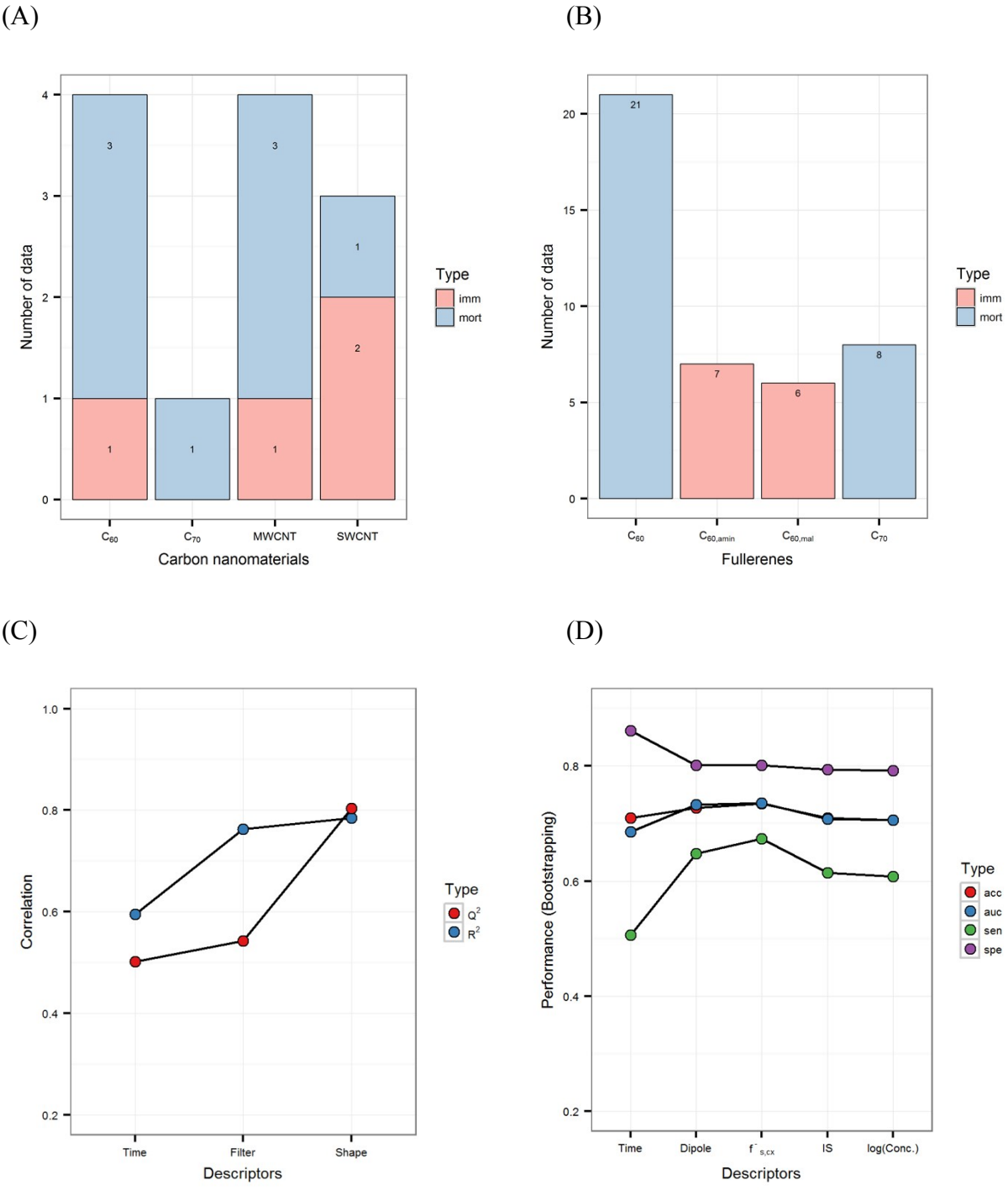


Figure S6. The number of pEC_{50} data for CNMs was only 12 (A), and that of class data was 42 (B). Time is exposure time, Filter is application of filter for dispersion of carbon nanomaterial

(CNM) and Shape is used to describe shape of each CNM. Shape is classified into three groups (sphere, tube and multi-wall). Dipole is dipole moment of fullerenes, $f_{s,cx}^{-}$ is electrophilic softness density of amino-γ cyclodextrin (amin) and malonate-γ cyclodextrin (mal), IS is ionic strength of the media, and log(Conc.) is concentration of fullerenes in log scale. R^2 was 78.47 and Q^2 was 80.40 in the regression model with Time, Filter and Shape (C). For classification model, accuracy was 72.7%, specificity was 80.1% and sensitivity was 64.8% with Time and Dipole in bootstrapping (D).

Table S1. Comparison of averaged pEC_{50} for NPs and non-NPs.

Name	Time (hour)	Nano particles				Non-nano scale particles			
		pEC_{50} (mmol/l)		TEM diameter (nm)		pEC_{50} (mmol/l)		Particle size (nm)	
		Mean	Std.	Mean	Std.	Mean	Std.	Mean	Std.
Ag	48	3.80	0.65	47.46	51.71	2.22	0.00	200.00	0.00
Cu	48	2.62	0.43	64.94	32.96	2.81	0.00	500.00	0.00
ZnO	504	2.42	0.10	60.00	42.43	2.43	0.00	200.00	0.00
ZnO	48	1.75	0.59	57.82	48.34	1.79	0.45	680.00	438.18
CuO	48	1.55	0.58	35.56	4.36	-0.45	0.00	1500.00	0.00
TiO_2	96	1.08	0.71	48.74	49.82	-0.66	0.17	375.00	176.78
TiO_2	48	0.61	0.56	21.69	10.42	-0.67	0.18	10000.00	0.00
Al_2O_3	48	-0.13	0.11	80.00	0.00	-0.69	0.00	90000.00	0.00

* Standard deviation (Std.)