Electronic Supplementary Material (ESI) for Nanoscale.

SUPPORTING INFORMATION

Parametrization of Nanoparticles: Development of Full-particle Nanodescriptors

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Supporting Information starts here:

Table 1. Formulas for calculating nanodescriptors for Metal Oxide nanoparticles.

GROUP 1: CONSTITUTIONAL DESCRIPTORS	
Total number of atoms in nanoparticle.	N
Total number of atoms in surface region of nanoparticle.	N_C
Total number of atoms in shell region of nanoparticle.	N_S
Total number of metal atoms in nanoparticle.	N_M
Total number of metal atoms in surface region of nanoparticle.	$N_{M,C}$
Total number of metal atoms in shell region of nanoparticle.	$N_{M,S}$
Total number of oxygen atoms in nanoparticle.	N_O
Total number of oxygen atoms in surface region of nanoparticle.	$N_{O,C}$
Total number of oxygen atoms in shell region of nanoparticle.	$N_{O,S}$
GROUP 2: POTENTIAL ENERGY DESCRIPTORS	
Average potential energy of all atoms in nanoparticle in electron volts.	E_P/N, where E_P is sum of potential energy of all atoms in nanoparticle
Average potential energy of atoms in surface region of nanoparticle in electron volts.	$E_{P,C}/N_C$, where $E_{P,C}$ is sum of potential energy of atoms in surface region
Average potential energy of atoms in shell region of nanoparticle in electron volts.	$E_{P,S}/N_S$, where $E_{P,S}$ is sum of potential energy of atoms in shell region
Average potential energy of metal atoms in nanoparticle in electron volts.	$E_{P,M}/N_M$, where $E_{P,M}$ is sum of potential energy of metal atoms in nanoparticle
Average potential energy of metal atoms in surface region	$E_{P,M,C}/N_{M,C}$, where $E_{P,M,C}$ is sum

of nanoparticle in electron volts.	of potential energy of metal atoms in surface region
Average potential energy of metal atoms in shell region of nanoparticle in electron volts.	$E_{P,M,S}/N_{M,S}$, where $E_{P,M,S}$ is sum of potential energy of metal atoms in shell region
Average potential energy of oxygen atoms in nanoparticle in electron volts.	$E_{P,O}/N_O$, where $E_{P,O}$ is sum of potential energy of oxygen atoms in nanoparticle
Average potential energy of oxygen atoms in surface region of nanoparticle in electron volts.	$E_{P,O,C}/N_{O,C}$, where $E_{P,O,C}$ is sum of potential energy of oxygen atoms in surface region
Average potential energy of oxygen atoms in shell region of nanoparticle in electron volts.	$E_{P,O,C}/N_{O,S}$, where $E_{P,O,C}$ is sum of potential energy of oxygen atoms in shell region
GROUP 3: TOPOLOGY DESCRIPTORS	*Coordination number of each individual atom is defined as the count of atoms which lie in the radius* $R=1.2*(R_M+R_O)$, R_M *and* R_O *are ionic radii of metal and oxygen atoms.*
Average coordination number of all atoms in nanoparticle.	C/N, where C is the sum of coordination numbers of all atoms in nanoparticle
Average coordination number of atoms in surface region of nanoparticle.	C_C/N_C, where C_C is the sum of coordination numbers of all atoms in surface region
Average coordination number of atoms in shell region of nanoparticle.	C_S/N_C, where C_S is the sum of coordination numbers of all atoms in surface region
Average coordination number of metal atoms in nanoparticle.	C_M/N_C, where C_M is the sum of coordination numbers of all metal atoms in nanoparticle
Average coordination number of metal atoms in surface region of nanoparticle.	$C_{M,C}/N_C$, where $C_{M,C}$ is the sum of coordination numbers of all metal atoms in surface region
Average coordination number of metal atoms in shell region of nanoparticle.	$C_{M,S}/N_C$, where $C_{M,S}$ is the sum of coordination numbers of all metal

	atoms in shell region
Average coordination number of oxygen atoms in nanoparticle.	C_O/N_C, where C_O is the sum of coordination numbers of all oxygen atoms in nanoparticle
Average coordination number of oxygen atoms in surface region of nanoparticle.	$C_{O,C}/N_C$, where $C_{O,C}$ is the sum of coordination numbers of all oxygen atoms in surface region
Average coordination number of oxygen atoms in shell region of nanoparticle in.	$C_{O,S}/N_C$, where $C_{O,S}$ is the sum of coordination numbers of all oxygen atoms in shell region
GROUP 4: SIZE DESCRIPTORS	
Diameter of the nanoparticle in Å.	D
Surface area of the nanoparticle in Å2.	$4\pi r^2$, where r is the radius of nanoparticle
Volume of the nanoparticle in Å3.	$4\pi r^3/3$, where r is the radius of nanoparticle
GROUP 5: LATTICE ENERGY DESCRIPTORS	
Lattice energy of nanoparticle in electron volts.	$(n_O+n_M)E_P/N$, where n_O and n_M are number of oxygen and metal atoms in metal oxide formula (e.g. 3 and 2 for Fe_2O_3)
Difference of the lattice energies of nanoparticle and infinite crystal.	$E_{L,I}$- E_L, where $E_{L,I}$- is the lattice energy calculated for infinite crystal (periodic calculation of 8 unit cells), E_L is the lattice energy of nanoparticle
Lattice energy of nanoparticle divided by the diameter of nanoparticle.	E_L/A, where EL is the lattice energy of nanoparticle and D is the diameter of nanoparticle
Lattice energy of nanoparticle per unit surface area.	E_L/A, where EL is the lattice energy of nanoparticle and A is the area of nanoparticle
Lattice energy of nanoparticle per unit volume.	E_L/A, where EL is the lattice energy of nanoparticle and V is the volume of nanoparticle

QNAR model development

The model development was carried out using the CODESSA PRO software.(www.codessa-pro.com) In the first step of feature selection, the most significant nanodescriptors were chosen from the pool of 35 descriptors according to the following criteria: correlation improvement cutoff – 0.02, max R^2 for orthogonal scales – 0.1, max R^2 for collinear scales – 0.6 For constructing two-parameter equations, pairwise selection was performed according to the criteria: inter-correlation coefficient in the pair below threshold (0.01), significant correlation with endpoint in terms of correlation coefficient and t-test.

The validation of sample model making use of the novel nanodescriptors was constructed based on the 17 metal oxide nanoparticles already modeled by Puzyn*, et. al.*[16(main paper)] Surface-modified particles and mixed oxides were not considered here, as these were out of scope of the present study. All of the particles were constructed as described in the methodology and the respective nanodescriptor values were calculated according to the sizes of the particles. The model was constructed using the best-multilinear algorithm (BMLR).

The resulting two-parameter model (*Sample 1*, Table 2, Figure 1) had the following equation:

$$log(1/EC_{50}) = 3.82 + 0.07D_1 - 0.05D_2, \qquad (1)$$

where D_1 is the descriptor "Average potential energy of atoms in shell region of nanoparticle" and D_2 is the "Average potential energy of oxygen atoms in surface region of nanoparticle", both given in electron volts. The statistical parameters of the model were found to be: squared correlation coefficient ($R^2 = 0.87$); squared cross validated correlation coefficient ($R^2_{cv} = 0.81$); Fisher criterion ($F = 45.26$); Squared standard deviation ($s^2 = 0.04$). The principal descriptor here was found to be D_1, which by itself was capable of accounting for most of the variability in the

dataset (one-parameter model with $R^2 = 0.83$). However, the two-parameter model, while only slightly higher correlating, was found to be more stable.

Table 2. Experimental and predicted *log(1/EC$_{50}$)* values of nanoparticles, calculated nanodescriptors and diameters for *Sample 1*.

	log(1/EC$_{50}$)		**Nanodescriptors**		**NP size**
NP	**Exp.**	**Pred.**	**D_1 (eV)**	**D_2 (eV)**	**Diameter (nm)**
Al_2O_3	2.49	2.49	-32.79	-20.8	31
Bi_2O_3	2.82	3.01	-17.04	-8.36	51
CoO	3.51	3.37	-19.83	-20.14	20
Cr_2O_3	2.51	2.68	-30.37	-21.09	20
CuO	3.2	3.34	-21.25	-21.6	48
Fe_2O_3	2.29	2.71	-29.64	-20.71	20
In_2O_3	2.81	2.75	-27.88	-18.94	59.6
La_2O_3	2.87	2.77	-12.12	4.24	24.6
NiO	3.45	3.37	-19.92	-20.33	20
Sb_2O_3	2.64	2.74	-28.04	-18.97	20
SiO_2	2.2	1.96	-41.98	-23.11	20
SnO_2	2.01	2.11	-37.23	-19.27	21
ZnO	3.45	3.38	-19.36	-19.7	21
ZrO_2	2.15	2.22	-32.16	-14.06	25
TiO_2	1.74	1.77	-43.31	-21.05	15
V_2O_3	3.14	2.72	-28.6	-19.47	20
Y_2O_3	2.87	2.75	-27.19	-18	32.7

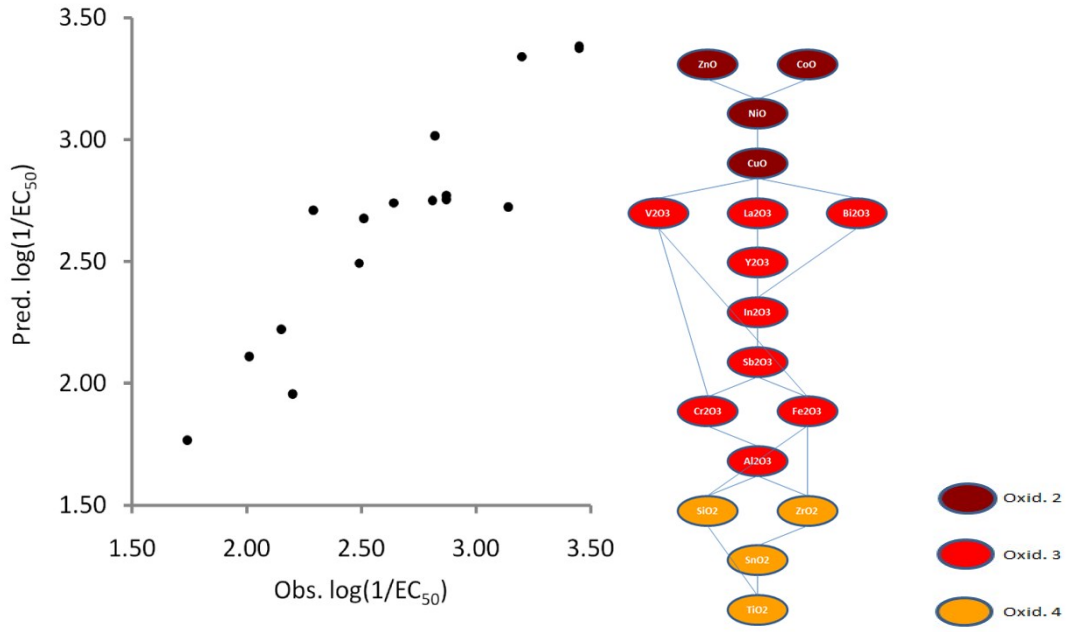

Figure 1. A: Plot of observed *vs.* predicted *log(1/EC$_{50}$)* values of metal oxide nanoparticles for *Sample 1.B: Ranks of the same values showing the overall oxidation stage of the metals ion (Rank correlation of 0.9)*