



Enalos QNAR Iron Oxide Toxicity Platform

A brief tutorial

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Overview

Online toxicity predictions for Iron Oxide nanoparticles (NPs) are made available through *Enalos QNAR Iron Oxide Toxicity Platform*.

Enalos QNAR Iron Oxide Toxicity Platform hosts a fully validated predictive model developed by NovaMechanics Ltd which generates toxicity predictions based on a set of indicated properties. Full documentation on the model development can be found in:

G. Melagraki and A. Afantitis, "A Risk Assessment Tool for the Virtual Screening of Metal Oxide Nanoparticles through Enalos InSilicoNano Platform", Current Topics in Medicinal Chemistry, vol. 15, no. 18, pp. 1827-36, 2015.

Enalos QNAR Iron Oxide Toxicity Platform is accessible through the following url:

http://enalos.insilicotox.com/QNAR_IronOxide_Toxicity/

The platform can be easily accessed, there is no need for authorization and the user can directly use the provided service.

The web service provides the functionality to virtually screen a set of NPs of interest based on the validated model, and thus yielding a preliminary *in silico* testing. Enalos Cloud Platform for NPs aspires to act as a useful aid within a virtual screening framework, for the design of novel NPs or the prioritization of novel potent NPs based on their predicted toxic effect.

Instructions

Required input

To initiate a prediction, the user must provide values for the four parameters below:


- NP size in nm
- Zeta Potential (ZP) in mV
- Relaxivities R1 and R2 in $\text{mM}^{-1}\text{s}^{-1}$

and, in addition, the user must indicate the coating among three alternatives:

- Cross-linked dextran
- Poly(vinyl alcohol) (PVA)
- Other



How to provide data for a given NP or a set of NPs (Figure 1)

 **Enalos QNAR Iron Oxide Toxicity Platform**

MNP Number	Size (nM)	ZP (mV)	R1 (mM-1S-1)	R2 (mM-1S-1)	Coating
1	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	Other ▾
2	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	Other ▾
3	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	Other ▾
4	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	Other ▾
5	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	Other ▾
6	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	Other ▾
7	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	Other ▾
8	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	Other ▾
9	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	Other ▾
10	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	Other ▾
11	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	Other ▾
12	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	Other ▾
13	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	Other ▾
14	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	Other ▾
15	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	Other ▾
16	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	Other ▾
17	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	Other ▾
18	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	Other ▾
19	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	Other ▾
20	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	Other ▾

Import a CSV file for High Throughput Virtual Screening (.csv)

No file selected.

Figure 1: Enalos QNAR Iron Oxide Toxicity Platform. At the top page the input form can be seen and at the bottom by clicking on “Browse” button, the user can import a .csv file with all the required properties.

The user has two alternative ways to provide the above information:

1. Directly manually submit in the online form (Figure 1, see blue arrow):

For only one entry: Each row corresponds to one NP. The user provides values for the four parameters (Size, ZP, R1, R2) by entering a value in the corresponding field of the first row and in addition selects from the drop down menu a coating among the alternatives (cross-linked dextran, PVA, other).

For multiple entries: Different rows correspond to many NPs. The user provides information as above and now fills in data for multiple rows each corresponding to one NP. When directly submitting data through the online form, multiple entries are available for up to 20 NPs.

2. Import a .csv file (Figure 1, see green arrow):

For one NP or for a set of NPs, all necessary information can be submitted via a .csv file by clicking the “Browse” button. The file must have a specific format (Figure 2) as described below:



Rows: In the first row the following column names should be included in the specific order: “row ID”, “Size”, “ZP”, “R1”, “R2” and “Coating_new”.

Columns: Data should be included in each of the six columns for as many rows as the number of NPs. Columns (1) – (4) contain numerical fields whereas Column (6) contains text.

Column (1): An id is given by the user for his internal use and identification of the NP when results are generated, Column (2): Value for the NP size is given in nm, Column (3): Value for the ZP is given in mV, Columns (4) and (5): Values for R1 and R2 are given in $\text{mM}^{-1}\text{s}^{-1}$ respectively, Column (6): A text is provided among three options: “cross-linked dextran”, “PVA” and “other”.

	A	B	C	D	E	F	G
1	row ID	Size	ZP	R1	R2	Coating_new	
2	1	32	5.9	21	54	cross-linked dextran	
3	2	74	-2.72	21	153	cross-linked dextran	
4	3	27	3.34	17	36	cross-linked dextran	
5	4	33	-19.5	22	49	cross-linked dextran	
6	5	36	-14	19	45	cross-linked dextran	
7	6	28	3.24	19	39	cross-linked dextran	
8	7	31	-9.46	23	59	cross-linked dextran	
9	8	31	3.64	19	49	cross-linked dextran	
10	9	24	-11.7	22	54	cross-linked dextran	
11	10	37	0.766	21	52	cross-linked dextran	
12	11	38	-20.7	21	62	cross-linked dextran	
13	12	38	-9.08	21	62	cross-linked dextran	
14	13	31	-3.61	19	49	cross-linked dextran	
15	14	28	-9.23	15	40	cross-linked dextran	
16	15	36	-21.9	36	122	cross-linked dextran	
17	16	31	-6.11	20	45	cross-linked dextran	
18	17	40	-12	15	30	PVA	
19	18	40	-7.57	15	30	PVA	
20	19	40	0.25	15	30	PVA	
21	20	40	-6.05	15	30	PVA	
22	21	20	-12.3	0.5	0.5	PVA	
23	22	20	-4.22	0.5	0.5	PVA	
24	23	20	-7.15	0.5	0.5	PVA	
25	24	20	-12.1	0.5	0.5	PVA	
26	25	20	-15.6	0.5	0.5	Other	
27	26	20	-16.1	0.5	0.5	PVA	
28	27	20	-4.7	0.5	0.5	PVA	
29	28	20	-6.47	0.5	0.5	PVA	
30	29	20	-10.8	0.5	0.5	Other	
31	30	23	-13.6	29	62	Other	
32	31	33	-14.5	36	106	Other	
33							
34							

Figure 2: Required format of the .csv file with a sample of input data.

By clicking the “Submit” button found under the online form or under the imported .csv file (Figure 1, see red arrows), depending on the method chosen to provide the input data, predictions for each NP are generated.



Predictions - Output

As described above, when properties are uploaded for a set of NPs, a prediction is generated by submitting the input values, the predictive model is then applied to the data provided and the output is generated within seconds (Figure 3).

OK Upload Is Successful! We are going to run nanoFe using IronOxides.csv Executed successfully 6
The results are
[Results.html](#) [Results.csv](#)

Figure 3: Generated output page. The user can select either to display the results in .html format or to download them in a .csv file.

To display the results, the user can then select among two options:

- “Results.html” option: the user can extract the results in a pdf-like format in a new html page,
- “Results.csv” option: the user can extract the results in a .csv file.

In both cases two columns are included, namely “Prediction” and “Domain” (Figure 4).

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"Prediction"	"Domain"
active	reliable
active	reliable
inactive	reliable
active	reliable
inactive	reliable

Date: Jan 27, 2017 11:44 AM
www.knime.org

Author: NovaMechanics Ltd

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Figure 4: Results table. The first column contains the prediction for each input NP and the second column contains the reliability of each prediction based on the model’s domain of applicability.

The “Prediction” column contains the toxicity prediction. The toxicity prediction is given by assigning a class to each of the submitted NPs. The class “active” and the class “inactive” are the two options that indicate a possible toxic or non-toxic effect respectively, for a given submitted NP, based on the predictive model.

The “Domain” column contains an indication on the reliability of predictions based on the model’s domain of applicability limits. Two options are available: The “reliable” option which indicates a prediction within the domain of applicability of the model and the “unreliable” option which is a warning for a prediction out of the domain of applicability of the predictive model.

If more NPs need to be submitted, the user can return to the initial page and by clicking on the “Reset” button next to “Submit” button the data are cleared and new input data can be submitted.

A demonstration video is available at:

https://www.youtube.com/watch?v=8Rxo_dhmD34