NANOINFORMATIX:
towards the implementation of a sustainable infomatics tool for engineered nanomaterials risk modeling … maximizing the value of data

Miguel A. Bañares (CSIC)

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EuroNanoForum 2019

Bucharest, Romania

EuroNanoForum 2019

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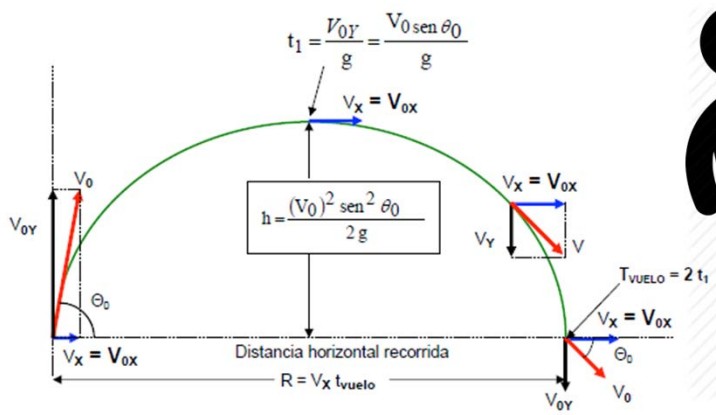
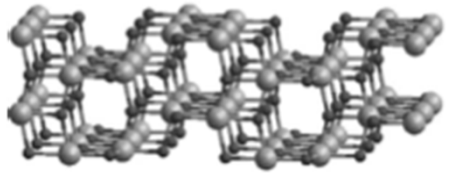
Nanomaterial toxicity: uphill on the complexity avenue





- Parabolic shot

Kick a peer

Take an aspirin

Nanoparticle

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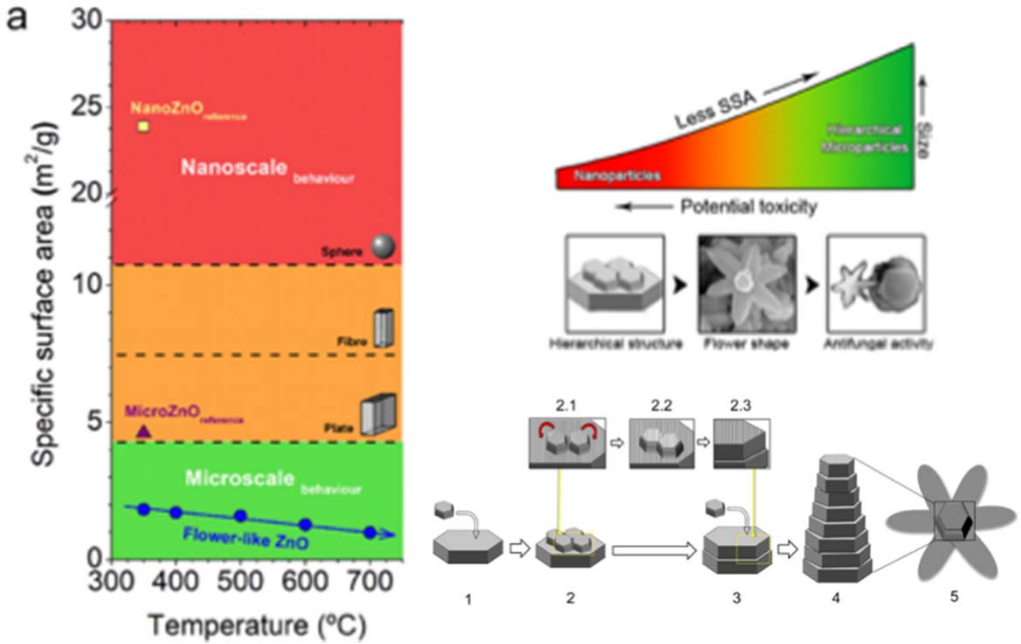
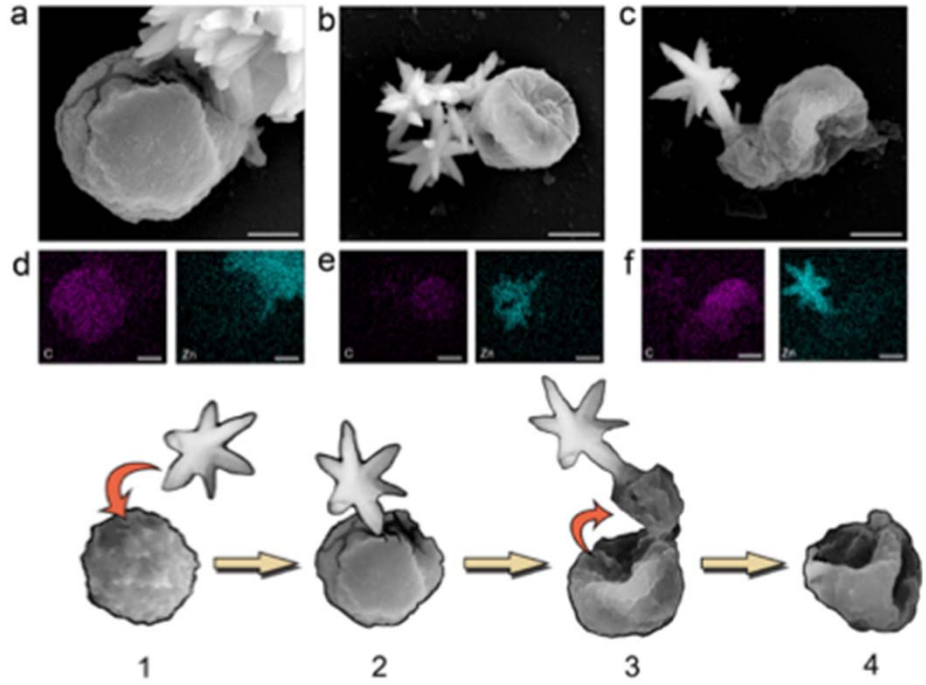
Good or bad: Toxic or Antibacterial ZnO

- Aspergillus Niger





de Lucas-Gil,. Materials & Design, 134(C), 188–195

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FAIR (Findable, Accessible, Interoperable, Reusable) data

- The nanoinformatics community (NanoInformatics Roadmap 2030) anticipates **multiple databases** administrated independently, while with some level of **interoperability**.

- The NanoInformaTIX database builds upon existing efforts of integrating NSC and external databases using eNanoMapper data solutions
  - https://search.data.enanomapper.net
- By using the **modular database architecture**, we will enhance the content both by data generated by project partners and integrating external databases through **the federated search layer**.
- Beyond manual data curation

NanoInformaTIX DATA

1. From completed EU projects (e.g. MARINA, NanoVALID, NanoSOLUTIONS, SUN, etc.) and established databases (e.g. eNanoMapper, DaNA and NanoWerk);
2. Emerging data from ongoing projects (NanoReg^2, CaliBRATE, PATROLS, GRACIOUS, BIORIMA);
3. North American projects (e.g. from NIOSH, UCLA, Duke University and Health Canada); Chinese projects (from the Chinese Academy of Sciences); South African projects (from MinTek) and curated peer reviewed literature.

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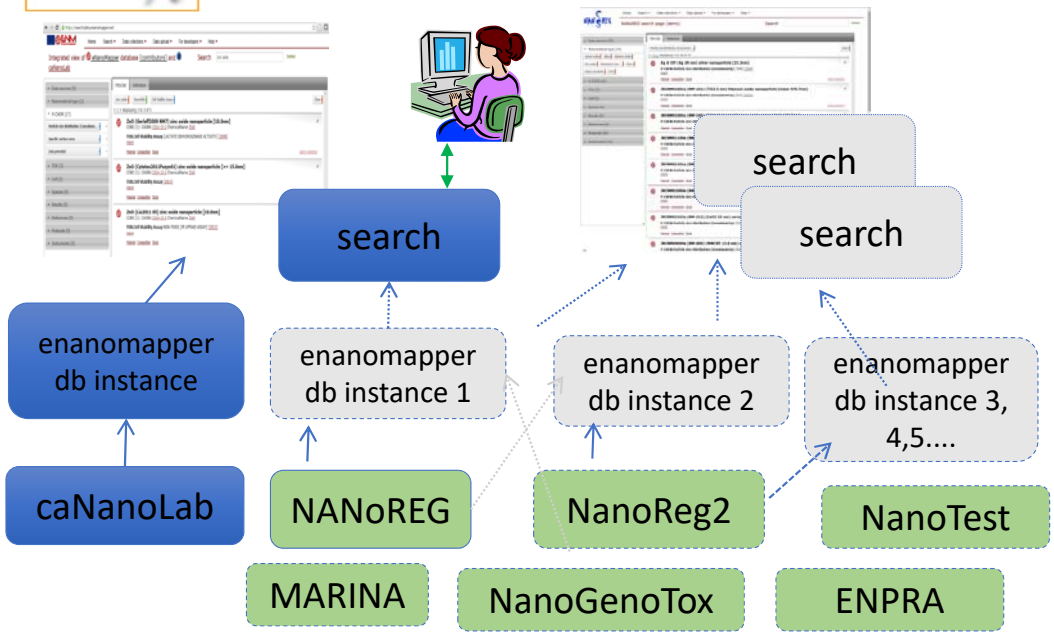
Reusable data @ https://search.data.enanomapper.net



Project	ENPRA	MARINA	NANoREG	NanoGenotox	NanoTest	*Total (Data points)*
ECOTOX		71	345			*416*
P-CHEM		268	12808	408	44	*13528*
TOX	3310	15694	26235	26341	13887	*85467*
Total	*3310*	*16033*	*39388*	*26749*	*13931*	*99411*

- Automated data import
  - e.g. MS Excel, OECD HT, ISA- TAB, IUCLID5/6
  - More that 1000 Excel files annotated and imported
- Different data formats supported (e.g. ISA-TAB, JSON, ISA-JSON). Conversions between data formats
- Plenty of search options (free text, faceted search, ontology terms). Protected access.
- Export options, web UI and API
- EUON https://euon.echa.europa.eu/enanomapper

Powered by open source eNanoMapper database (backend) , open source JS https://github.com/ideaconsult/jToxKit (frontend)

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A glimpse into data content

https://search.data.enanomapper.net

Row Labels	MARINA	NanoGenotox	NANoREG	NanoReg2	NanoTest	Grand Total
4.1. Appearance						
4.19. Stability (thermal)	5					
4.24. Nanomaterial agglomeration/aggregation	8					
4.25. Nanomaterial crystalline phase	4					
4.26. Nanomaterial crystallite and grain size	5					
4.27. Nanomaterial aspect ratio/shape	8					
4.28. Nanomaterial specific surface area	5					
4.28.12. Radical formation potential	1					
4.29. Nanomaterial zeta potential						
4.30. Nanomaterial surface chemistry	5					
4.31. Nanomaterial dustiness	3					
4.32. Nanomaterial porosity	5					
4.4. Density	7		3			
4.5. Particle size distribution (Granulometry)	29	1	1878			
4.8. Water solubility			94			
4.9. Solubility in organic solvents			5			
4.99. Physico chemical properties (other)						
CHMO_0001075. Analytical Methods	49	1	85			
ENM_0000081. Batch Dispersion quality			168			
ENM_8000223. Aerosol characterisation			29			
Grand Total	**134**	**12**	**2787**	**24**	**55**	**3012**

Row Labels	ENPRA	MARINA	NanoGenotox	NANoREG	NanoTest	Grand Total
7.5.1. Repeated dose toxicity - oral			859	168		1027
7.5.2. Repeated dose toxicity - inhalation		55		46		101
7.6.1. Genetic toxicity in vitro	33		1409	638	28	2108
7.6.2. Genetic toxicity in vivo				52		52
BAO_0002189. Toxicity (other)		6			14	20
ENM_0000037. Oxidative Stress	11	16		68	55	150
ENM_0000044. Barrier integrity		7		130		137
ENM_0000068. Cell Viability	126	136	75	979	106	1422
NPO_1339. Immunotoxicity		15		232	35	282
Grand Total	**170**	**235**	**2343**	**2313**	**238**	**5299**

Row Labels	MARINA	NANoREG	Grand Total
6.1.1. Short-term toxicity to fish	21		21
6.1.3. Short-term toxicity to aquatic inverterbrates	8	30	38
6.1.5. Toxicity to aquatic algae and cyanobacteria	1	20	21
6.2. Sediment toxicity	1		1
6.3.1. Toxicity to soil macroorganisms		12	12
6.3.3. Toxicity to terrestrial plants	7		7
6.3.4. Toxicity to soil microorganisms	11		11
Grand Total	**49**	**62**	**111**

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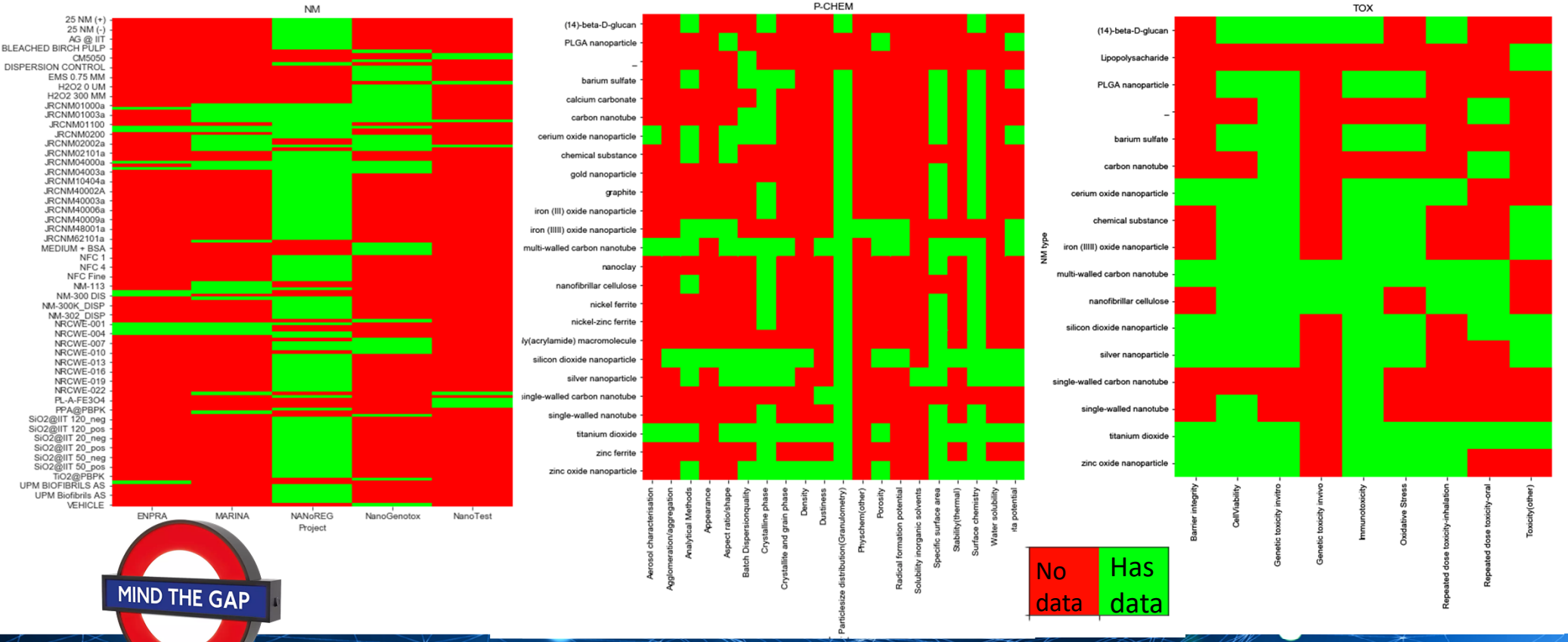
Automatic data gaps analysis by Jupyter Notebooks



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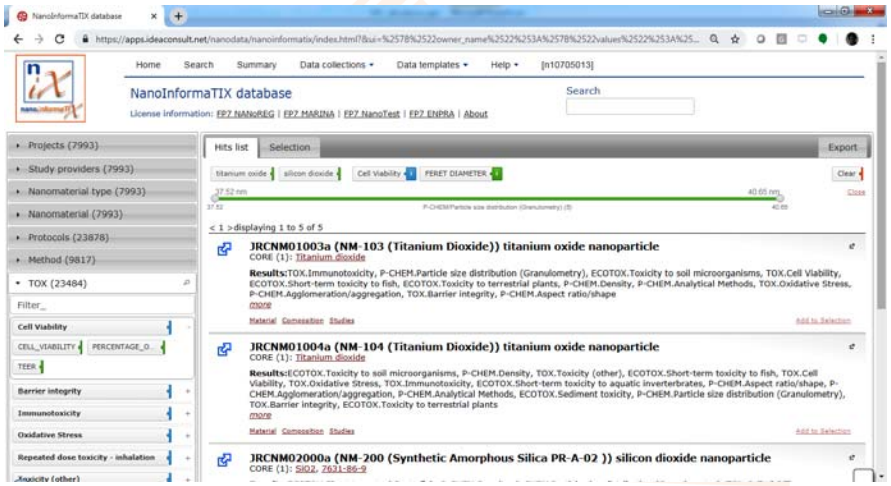
Experimental data and material modeling



MODELS

NanoInformaTIX will develop and extend existing models - some created in recent modelling projects (NanoSOLUTIONS, MOD-ENP-TOX, MODERN, PRENANOTOX, MEMBRANENANOPART, NANOPUZZLES and the COST Action TD1204 MODENA) or projects with a modelling component (e.g. ENPRA, MARINA).

Materials modelling

Exposure modelling

Bio-distribution modelling

Dose-Response modelling

- Open source libraries for data access
- Integration of data analysis methods for data curation and data exploration
- Support material modelling
  - Material selection
  - Models Input and output

SNF will be co-implemented together with **stakeholders** to ensure a user-friendly interface for industry, regulators, researchers and civil society, providing cost effective safety assessment guidance.

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BEYOND CLASSICAL AGGREGATION THEORY

> Predictive DLVO-like theory but for realistic environments (DLVO stands for Derjaguin, Landau, Verwey, and Overbeek)

> Nanotoxicity depends on an enormous amount of parameters, but some of them has proved to be particularly relevant, e.g. hydrophobicity / hydrophilicity, aggregation, protein binding and interaction with membranes

> This seems to suggest that potential of mean force (PMF) is important for predicting nanotoxicity

> The classical theory for predicting PMF of nanoparticles is the DLVO theory, but it shows some limits. First of all, non-continuum (discrete) effects are neglected. Moreover, the DLVO theory depends on two inputs, namely the Hamaker constant and the surface partial charge

> KEY POINT: It would be very important to develop a predictive theory for assessing the surface partial charge as a function of the solvation environment, which depends on ion concentration, ion dissociations, pH, etc.

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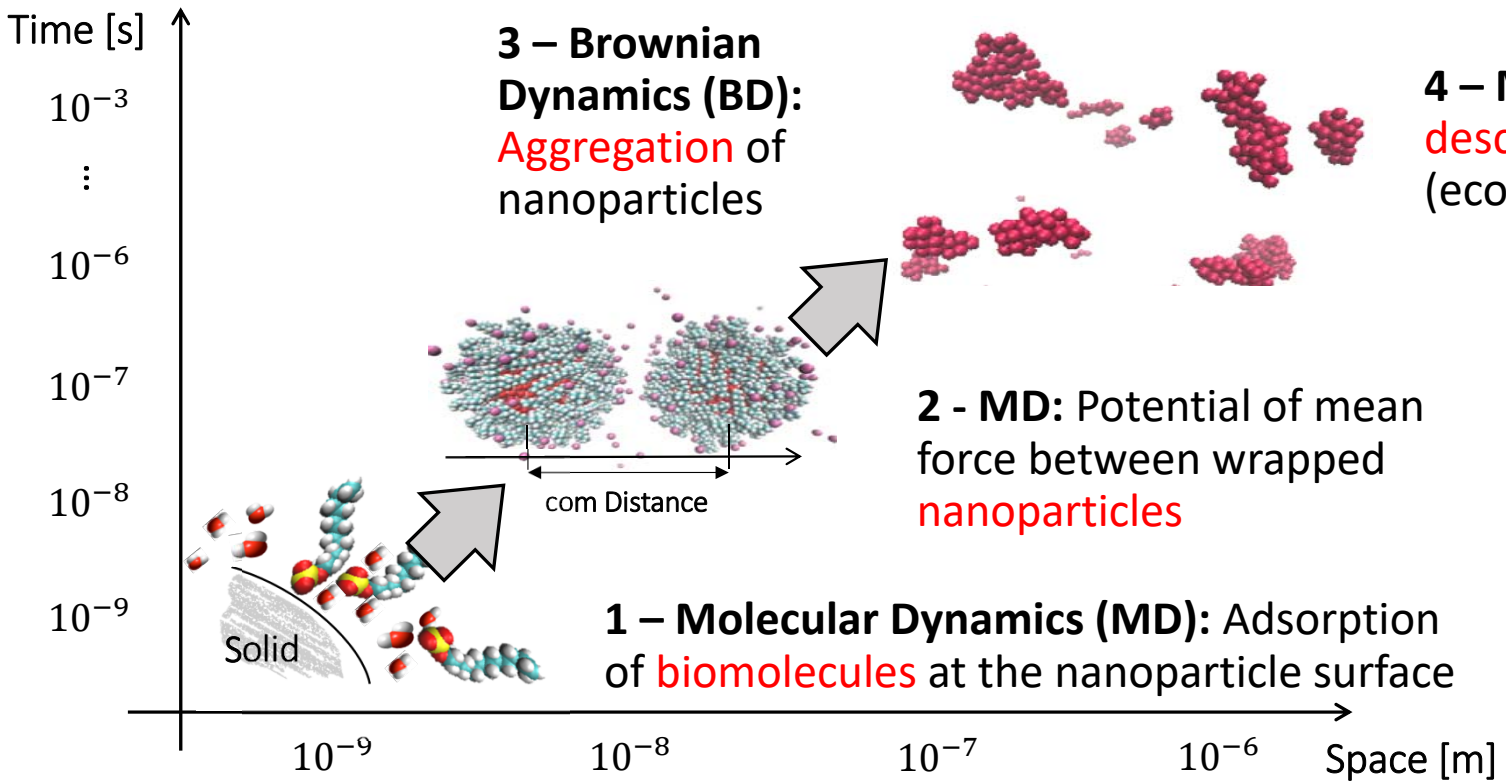
SEQUENCE OF LINKED MODELS



3 – Brownian Dynamics (BD): Aggregation of nanoparticles

4 – Mean Field Theory: New descriptors for assessing (eco)nanotoxicity

2 - MD: Potential of mean force between wrapped nanoparticles

1 – Molecular Dynamics (MD): Adsorption of biomolecules at the nanoparticle surface

A. Cardellini *et al.* Nanoscale 9, 2019

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Endowing data with value

> **Enables predicting**

- ✓ Exposure and Bio-Distribution Modelling
- ✓ Dose-Response Modelling
- ✓ Model validation and integration

>_ **NanoInformaTIX** will bring predictive toxicology knowledge to enable engineered nanomaterials (ENM) sustainable production through:

- ✓ reduction of animal experimentation
- ✓ Safe-by-Design
- ✓ Grouping/classifying for risk assessment of ENM

>_ The SNF will become a **global hub for ENM safe-by-design**, a portal for manufacturers and scientists to go to for information on their materials.

>_ The SNF enabling technology will help shortening considerably the path from lab bench to the market offering a **tangible product that can be used and upgraded in the future**.

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Broad outreach of data value

Industry

speed, cost-effective production, use of safe-by-design which anticipates uncertainties and risks early in the innovation process, helping industries to be more competitive

Regulators

sound, validated methodologies

Consumers

safer and better products on the market, transparency and trust

Researchers

availability of tools to turn research into successful products

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Thank you for your attention !

www.nanoinformatix.eu

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Data will enable a sustainable platform for predictive toxicolgy

> WP1_ Project management and Coordination

> WP2_Data and database

> WP3_Nanomaterials and Material Modelling

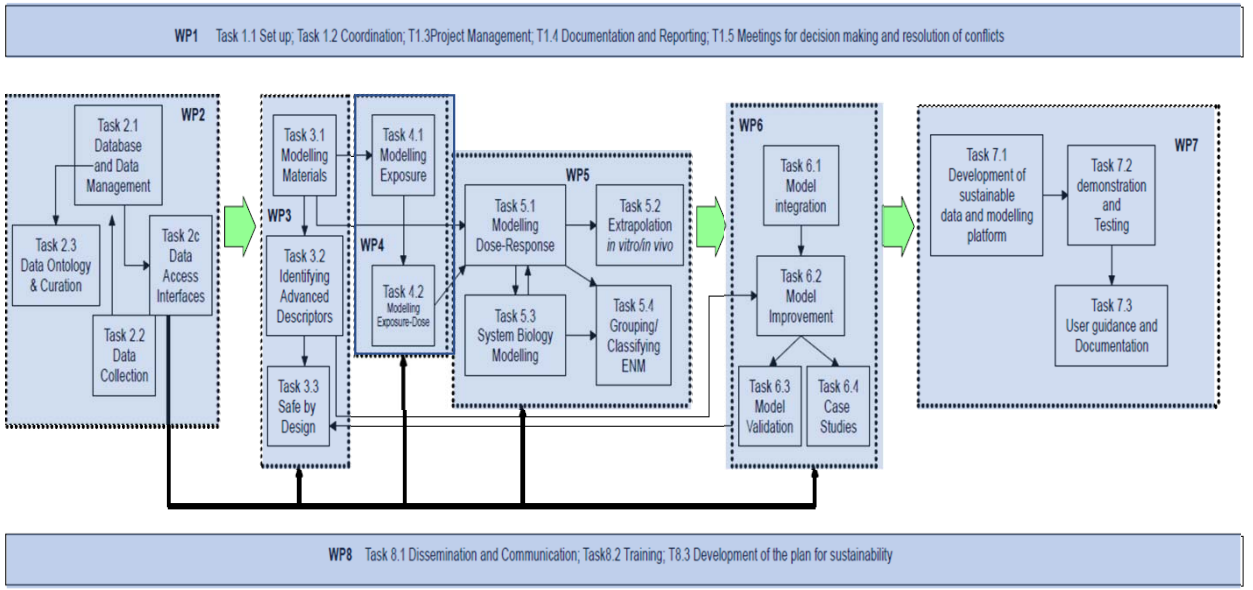
> WP4_Exposure and Bio-Distribution Modelling

> WP5_Dose-Response Modelling

> WP6_Model validation and integration

> WP7_ Implementation of a sustainable SNF Platform

> WP8_Dissemination, Exploitation, Training



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MATERIALS MODELLING

Objective #1
to develop a material modelling framework which couples/links different models for assessing ENM physicochemical properties

Objective #2:
to develop advanced descriptors for the evaluation of ENM exposure/hazard, in particular ENM (i) persistence, (ii) aggregation and (iii) interactions with the environment/target, which will include intrinsic descriptors (i.e. system independent) and extrinsic descriptors (i.e. system dependent properties)

Objective #3
to develop a Safe-by-Design approach for ENM

MATERIALS MODELLING effectively used for improving the (eco)nanotoxicity assessment of ENM

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