Hazard mechanisms, biokinetics & vulnerable populations

Éva Valsami-Jones **NanoMILE**

Brussels, 10-11 December 2014

Hazard mechanisms, biokinetics & vulnerable populations: science shaped around the Strategic Research Agenda

Reflections of the past

Brussels, 10-11 December 2014

NanoSafety Cluster

Highlights from project NanoReTox

Brussels, 10-11 December 2014

NanoReTox investigated:

- 8 inorganic MNM classes
  - TiO_2, CuO, Ag, Au, ZnO, SiO_2, CdS, CdSe NPs along with aqueous and bulk counterparts
- 55 types of MNMs (range of sizes, coatings, shapes, both lab & commercial)
- 33 types of *in vitro* dose response tests with 6 different types of cells
- 23 types of *in vivo* dose response tests
- 8 species + human cells of various types

SEVENTH FRAMEWORK

NanoReTox

UNIVERSITY OF BIRMINGHAM

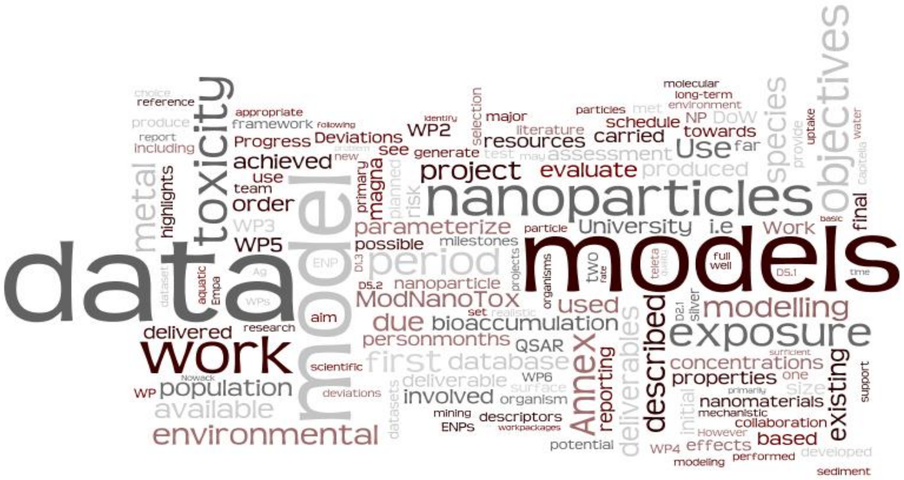
NanoReTox conclusions

Key conclusions

- Measures in reactivity do not seem to explain differences completely
- Chemical composition primary variant
- Order of aggregation/solubility does not follow order of toxicity
- Nanoeffect is there, but it is not off-scale

NanoSafety Cluster

Highlights from project ModNanoTox



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ModNanoTox unique features

Range of models & scales

- Molecular simulation models.
- Database of evaluated literature.
- Toxicokinetic/toxicodynamic models.
- QSAR models.
- Environmental exposure assessment models.
- Ecosystem effects, population models.

SEVENTH FRAMEWORK

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Hazard mechanisms, biokinetics & vulnerable populations: science shaped around the Strategic Research Agenda

Reflections into the future

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Latest project: Libraries (The NanoMILE library)

7 main families of materials selected

Nanomaterial	Justification for selection	Key descriptors	Surface functionalisation
CeO_2	Low solubility -> low toxicity Redox variations Isotopic label available Commercial value	Redox state Size Shape Solubility	Indirect - variation of stabilizing polymers
ZnO	High solubility -> high toxicity Isotopic label available High commercial value	Size Shape Dissolution rate / coating	Hydrophillic Hydrophobic
Ag	Variable solubility -> variable toxicity Isotopic label available High commercial value	Size Shape (including flowers) Dissolution rate / coating Surface defects	Citrate Tannic acid Fulvic acid Humic acid
SiO_2	Easily fluorescently labelled Multiple synthesis routes Low toxicity generally, though evidence that structural transformations can induce toxicity (e.g. fumed silica)	Size Porosity	- unmodified -COOH $-NH_2$ -(epoxy)
TiO_2	Low solubility -> low toxicity Multiple coatings available Different crystal phases Commercial value Photoreactive	Crystal structure / phase Coating (ageing) Size ROS production	- Uncoated - PVP - Pluronic F127 - Dispex AA4040
Fe_xO_y	Likely low solubility -> low toxicity Multiple structures & Magnetic properties Potential for labelling Medical applications	Crystal structure / phase Magnetic properties Coating Size	- uncoated - Dextran - PEG
CNT, Graphene or other carbon based MNM	High commercial relevance (e.g. Graphene Flagship) Non-spherical -> potential for alternative mechanisms of action	Aspect ratio Shape / structure C/O ratio / surface groups Surface functionalisation	CNT CNT-COOH $CNT-NH_2$(?)

Establishment of Nanoparticle Library (>150 variations from 7 main families)

Latest projects: selection of MNMs

Hypothesis focus

•Very small size (to follow quantum confinement etc effects): Au, Ag, TiO_2

•Surface functionalisation (systematic, wide-range): SiO_2 (+ve, -ve, naked, hydrophobicity/philicity), spions

•Solubility: Fe-doped ZnO, ultrastable Ag

•Redox potential: Zr-doped ceria, Fe-oxides

Predictive nanotoxicology & read-across

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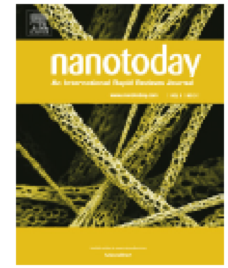

NEWS AND OPINIONS

A strategy for grouping of nanomaterials based on key physico-chemical descriptors as a basis for safer-by-design NMs

CrossMark

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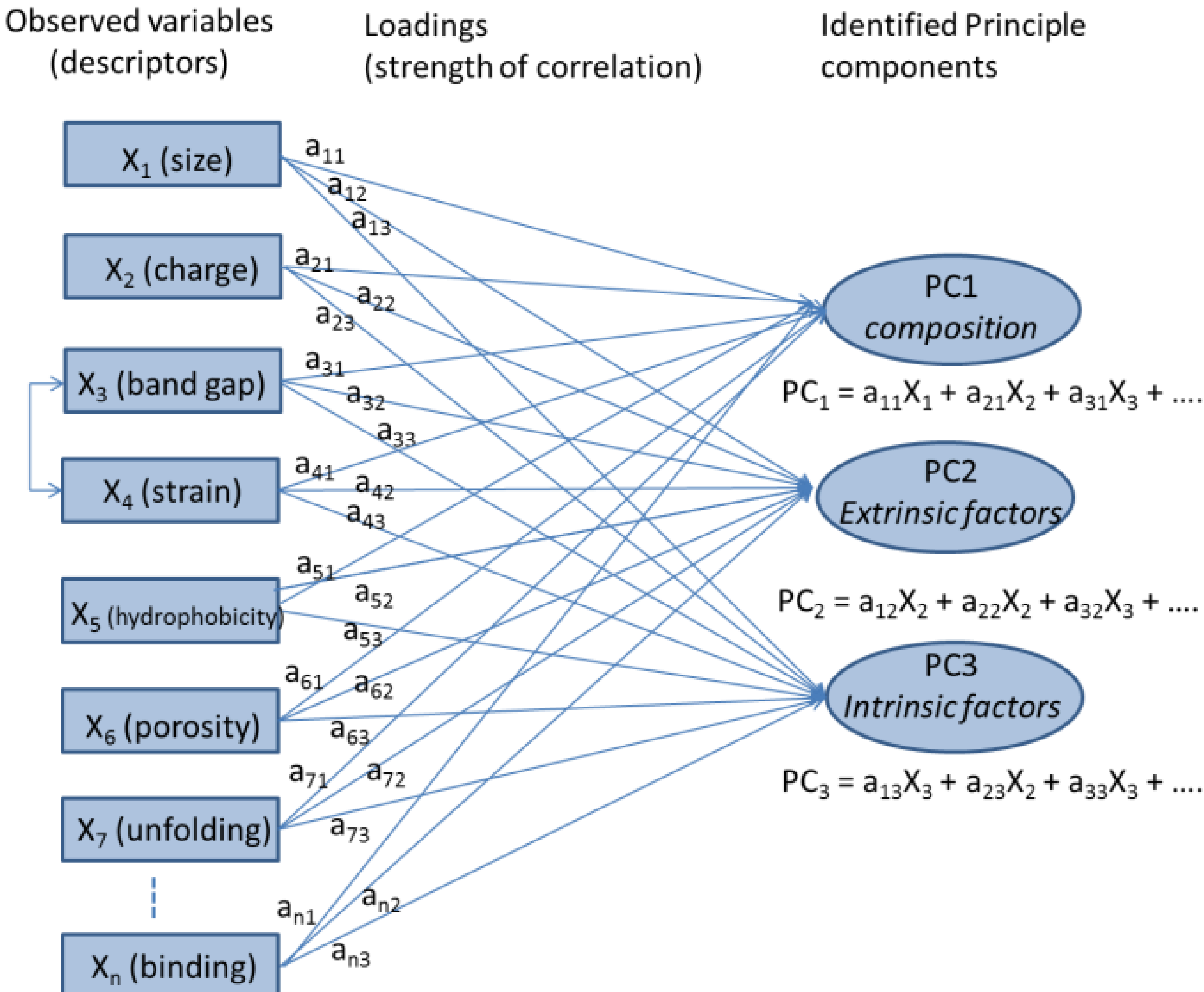
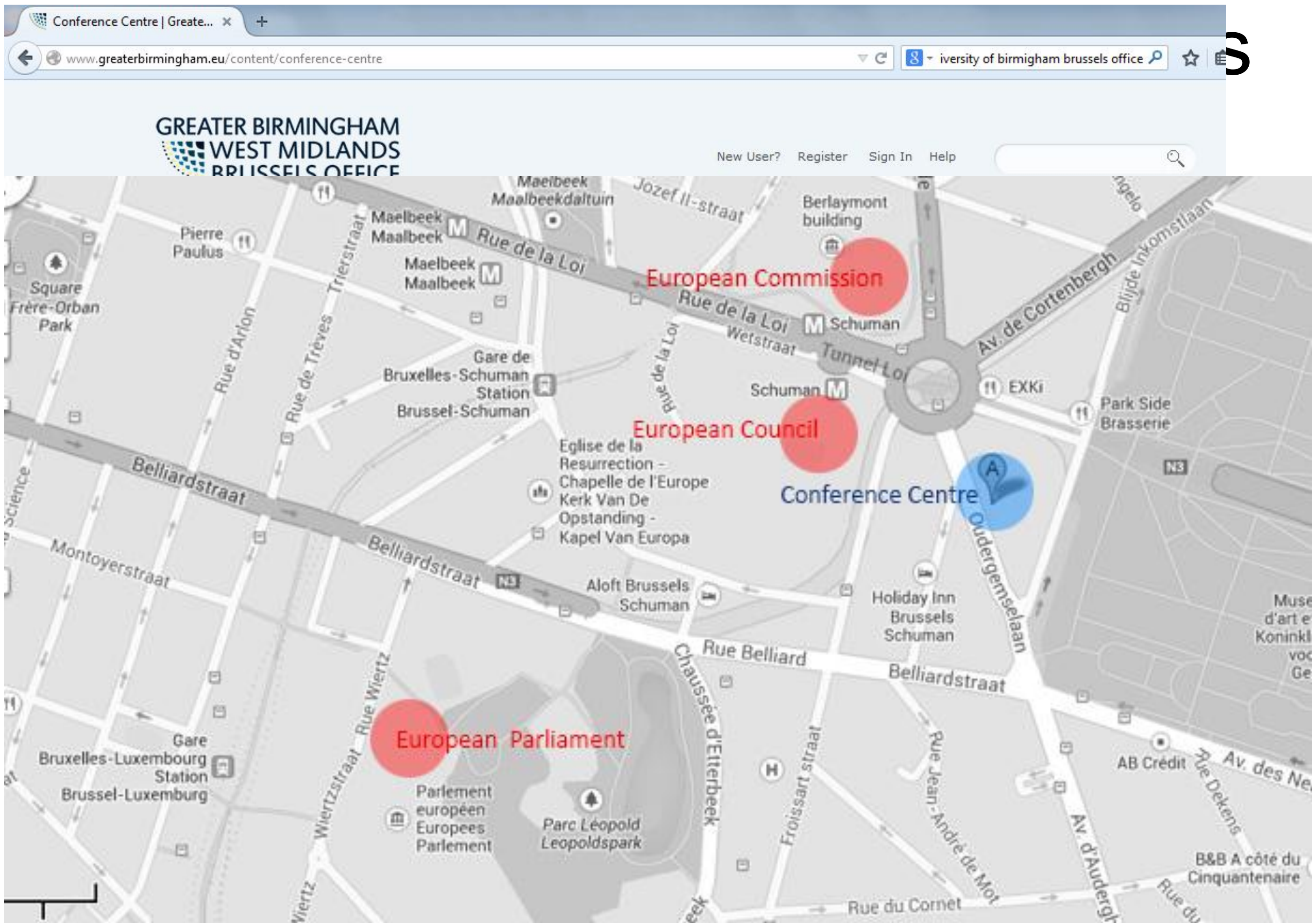
Predictive nanotoxicology & read-across



NSC WORKSHOP SERIES

- Proposing as the “Brussels nanosafety
  s



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NSC “Brussels” WORKSHOP SERIES

- Proposed topics for workshops

  - Methodologies for phys-chem / biophys-chem characterisation

May 2015

  - Data curation & tools for interrogation of data / risk assessment

October 2015

  - Alternative test methods – high throughput & omics approaches

May 2016

NSC "Brussels" WORKSHOP SERIES

- Implementation approach & approximate

Lead projects assign workshop coordinators from their consortia

Workshop coordinators agree scope & plan call for "data" inputs & participation

Call for relevant data sets & registration for 2.5-day workshop

Workshop coordinators compile inputs and draft white paper for discussion

6 months prior to workshop → 4 months prior to workshop (p2w)

Workshop coordinators identify discussion leaders for workshop

Workshop coordinators send draft white paper to participants

2.5 day workshop with experts to discuss & finalise white paper / publication

Final polishing by workshop coordinators prior to publication

2 months p2w → 1 month p2w → 1 month post workshop

NSC “Brussels” WORKSHOP SERIES

- Outputs from each workshop would be:
  - White paper & associated summary publication
  - Agreed terminology for the topic
  - Agreed protocols and approaches
  - Agreed understanding of current limitations of the methods / approaches in terms of their applicability to different NMs classes
  - Plan for benchmarking activities and buy-in of relevant projects with capabilities to achieve this
  - Perhaps more

NSC "Brussels" WORKSHOP SERIES

- Key questions

1. Can the white papers / standardised approaches be "charged for" ?

   i.e. at NanoMILE ESS had interesting discussion

   regarding whether agreed protocols could be sold as per BSI, ISO etc.?

   - idea would be that money generated rolls-back into NSC for subsequent workshops events

2. Internationalisation? Do we already want to invite experts from outside EU to the workshops?

THANK YOU!