Ontology Nanomaterials safety

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Knowledge development – difference in philosophy

Human readable format
• Provide database
• End-user builds knowledge.

Machine readable format
• Provide expert system
• End-user is presented with an answer.

• In reality, perhaps both?
Ontology

• A formal representation of a set of concepts and their relationships, linking facts to related terms in a **causal** order

• To formulate domain knowledge and integrate knowledge from diverse domains
  - Gene ontology
  - ChEBI (chemical entities of biological interest)
    • [http://www.ebi.ac.uk/chebi/](http://www.ebi.ac.uk/chebi/)
  - NPO for Cancer Nanotechnology Research
    • [http://www.nano-ontology.org/](http://www.nano-ontology.org/)
  - Toxicology ontology
A quick look at NanoParticle Ontology (NPO)

...to represent the knowledge underlying the description, preparation, and characterization of nanomaterials in cancer nanotechnology research in NCI...

doi: [10.1016/j.jbi.2010.03.001](http://dx.doi.org/10.1016/j.jbi.2010.03.001).

http://bioportal.bioontology.org/visualize/45233/
Example: Ontologies can be useful
Conceptual framework of chem-tox ontology
Example: the power of ontology from biological perspective

- Mutations and cancer endpoints are affected by genes in cell cycle and cell cycle checkpoint

[Diagram showing the relationship between cell cycle and cell cycle checkpoint]

http://www.geneontology.org/GO.ontology.relations.shtml
Example: the power of ontology from chemical perspective

- Flavonoids is an important chemical class in foods and drugs
  - phenol undergoes oxidation reaction
  - Role: often used as an antioxidant
Mechanistic reasoning by gene and chemical ontologies

- Flavonoid class is highly associated with gene expression of CDC25A, CDK, etc. (NCI/DTP data mining)
- Flavonoids are small molecule inhibitors
  - Requires hydrogen bonding in the pocket.
  - Oxidation of phenols adversely affects.
Knowledge Representation Ontology

- independent
- dependent (relative)
- mediating
- physical (object)
- abstract (description)

The Lattice

- continuant – thing/object
- occurrent – process
- thematic role – role

Nanoparticles safety ontology

• Framework
  – subatomic particles → atoms → molecules → nanoparticles → mesoporous particles → ....

• To model ENM interactions at the biological interface
  – Nano materials identification and characterization
  – Biological interface characterization

• To represent *in vitro* toxicity data and link to *in vivo* data
Knowledge discovery - food intake

synthesis

Microwave-Based Quantum Dot Synthesis

identification/characterization

biological characterization

in vitro model

STOMACH
pepsin/HCl pH 2

SMALL BOWEL
trypsin, lipase, carboxypeptidase, aminopeptidase, amylase, pH 7

biological process
Knowledge discovery – biological interface

- To model simple/plausible modes of ENM interactions with biological systems involved in safety

protein

particle surface

soft protein corona on particle surface

protein deactivation or denaturation

membrane disruption or lipid peroxidation

Toxicity potential
Representing things and happenings...

- **physical thing - object**
  - particle core
  - particle surface
  - medium
  - cells
  - proteins
  - lipid membrane

- **abstract things - property**
  - chemical make-up
  - charge
  - size
  - spectra/microscopy
  - ....

- **happening - process**
  - adsorbs
  - binds
  - catalyzes
  - decomposes
  - reacts
  - ....
Identification/Characterization of Nanomaterials

Nano-structured material

Materials Identifiers:
- XRD, XPS, TEM, IR...
- Chemical types

Physicochemical properties:
Bulk/surface

Chemical make-up:
Bulk/surface

- Stability
- Reactivity
- Biological activity

Dosimetry

Potential Toxicity

Things
- Neat
- Interface
  - Delivery system
  - Biological system
- Particle size
- Surface area
- Morphology
- Charges...

Altamira LLC
Classes in nano (particles or ENMs) ontology

- Particle
- ParticleAtInterface
- ParticleBiologicalReactivity
- ParticleChemicalReactivity
- ParticleCompositions
- ParticleIdentifier
- ParticleName
- ParticleMorphology
- ParticleRole
- ParticleSize
- ParticleSurfaceArea
- ParticleSurfaceCharge
- ParticleSurfaceTreatment
- ParticleStability
- MethodCellularAssay
- MethodPhysChem
- MethodSpectroscopy
- MethodMicroscopy
Simple example: classification

TiO$_2$

size 21 nm

XRD spectrum

TEM image

TiO$_2$ (particle)

TEM image

(Identifier)

XRD spectrum

(Identifier)

avg. 21 nm (size)
TiO$_2$
avg. 21 nm
XRD spectrum
TEM image

+ Entity
  + object
    + dependent
    + independent
    + spatial region
  + process
    + process entity
    + spatio-temporal
    + temporal
Back to NPO example

TiO$_2$
size 21 nm
XRD spectrum
TEM image

+ Entity
  + object
    + dependent
    + independent
      + material entity
        + nanomaterial
        + nanoparticle
        + metal oxide
    + spatial region
  + process
Back to NPO example

TiO$_2$
size 21 nm
XRD spectrum
TEM image

+ Entity
  + object
    + dependent
    + independent
      + material entity
        + nanomaterial
          + nanoparticle
          + metal oxide
      + spatial region
    + process
TiO$_2$
size 21 nm
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  + object
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    + material entity
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      + nanoparticle
        + metal oxide
    + spatial region
  + process
TiO\textsubscript{2} size 21 nm
XRD spectrum
TEM image
TiO$_2$
size 21 nm
XRD spectrum
TEM image

+ Entity
  + object
  + process
    + process entity
    + process
    + biological process
    + imaging
    + procedure
      + experiment
      + technique
        + microscopy
        + spectroscopy
    + spatiotemporal region
    + temporal region

procedure: imaging, microscopy, spectroscopy...
ChEBI: chemical entities of biological interests

+ subatomic particles

+ role:
  + application
  + biological
  + chemical

+ chemical entity:
  + atom
  + chemical substance
  + group
  + molecular entity
ChEBI framework – can we insert nano content?

+ subatomic particle
+ role
  + application
  + biological role
  + chemical role
  + ENMparticle role
+ chemical entity
  + atom
  + chemical substance
  + mixture
  + pure
  + ENMparticle
  + group
  + molecular entity
+ entity descriptions
  + spectroscopy
  + microscopy
  + morphology
  + surface
  + chemical make-up
+ process
  + biological process
Database – nanomaterials and toxicity endpoints

Particle Identification
Characterization

In vitro and In vivo assays
### Classification of nano-particles

<table>
<thead>
<tr>
<th>Clusters</th>
<th>Particles</th>
<th>XRD patterns</th>
<th>TEM/SEM images</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metal oxides</td>
<td>TiO$_2$</td>
<td><img src="image1" alt="XRD pattern" /></td>
<td><img src="image2" alt="TEM/SEM image" /></td>
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<tr>
<td></td>
<td>CeO$_2$</td>
<td><img src="image3" alt="XRD pattern" /></td>
<td><img src="image4" alt="TEM/SEM image" /></td>
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<td>Zeolites</td>
<td>Erionite</td>
<td><img src="image5" alt="XRD pattern" /></td>
<td><img src="image6" alt="TEM/SEM image" /></td>
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<td>SWCNT</td>
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<td><img src="image7" alt="XRD pattern" /></td>
<td><img src="image8" alt="TEM/SEM image" /></td>
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<tr>
<td>Quantum dots</td>
<td>CdSe/ZnS</td>
<td><img src="image9" alt="XRD pattern" /></td>
<td><img src="image10" alt="TEM/SEM image" /></td>
</tr>
</tbody>
</table>
2-D clustering of 12 nanoparticles against cytotoxicity and TNF-alpha

The color intensity (the 3rd dimension) indicates activity of biological assays including inflammation (TNFalpha). This is a data mining result from a database compiled from comprehensive literature searching as of 2010 January.

Descriptors
- chemical make-up
- XRD patterns
- TNF-alpha activity

_XRD(2θ) pattern_
In summary

• We as a field need to conduct “knowledge discovery” exercises to build an ENM ontology before we start stuff things into technology (OWL or RDF).

• Nanomaterials database based on meaningful data model is a pre-requisite to QNTR. Ontology driven data model would be highly desirable.
  – ENM Identifier
  – Minimum set of common entities for acceptable studies
  – Design of experiments (DOX, DOE)

• Nanomaterials will force us to free ourselves from connection table driven QSAR.
  – BACK TO THE PROPERTY SPACE!
Collaborators in nano ontology and nano safety

- Mitchell A. Cheeseman
- Prabir Dutta, James Rathman, James Waldman - the Ohio State University (US NIFA/Nano STAR)
- Andrew Worth, JRC