The NanoParticle Ontology for Nanoinformatics

Dennis G. Thomas, Nathan A. Baker

Knowledge Discovery and Informatics Group Pacific Northwest National Laboratory E-mail: <u>nathan.baker@pnl.gov</u>



PNWD-SA-9162

Introduction to vocabulary in nanoinformatics

- NanoParticle Ontology design
- NanoParticle Ontology applications
- Future growth and development

What is an ontology?

- Not a disease!
- Specification of logical relationships between concepts
- Also usually includes definitions, synonyms, properties, etc.

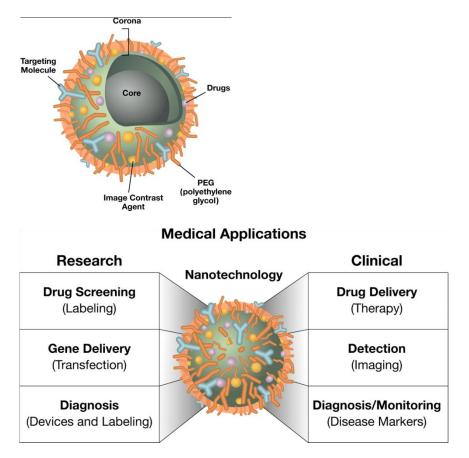
Other popular vocabularies:

Gene ontology MeSH ChEBI UMLS SNOMED Omega NCI Thesaurus RadLex Foundational Model of Anatomy MGED Ontology



Nanotechnology: promise and problems

- Nanomaterials are small and diverse
- The promise:
 - High density
 - Improved biodistribution
 - Multi-modal applications
- The problems:
 - Combinatorial diversity
 - Difficult characterization
- An important informatics challenge!

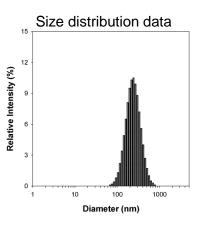


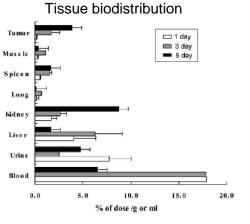
McNeil SE. *J Leukoc Biol*, 2005. **78**(3): p. 585-94. doi:10.1189/jlb.0205074



Why are Nanoparticles "Different"? Diversity of Data! Anti-tumor activity

5000

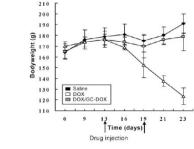


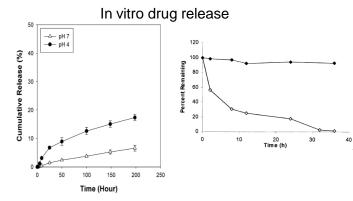


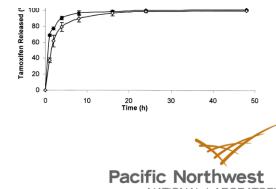
Saline 4500 DOX DOX/GC-DOX 200 \$ 4000 190 E 3500 B 3000 Po 2500 b 2000 140 E 1500 130 1000 120 500 110 16 19 21 23

Time (days)

Drug injection







NATIONAL LABORATORY

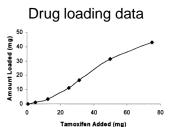
Zeta Potential

Table 1 Zeta potential values of control and tamoxifen loaded nanoparticles

Nanoparticle formulations	Zeta potential (mV)
Control nanoparticles Tamoxifen-loaded nanoparticles	$\begin{array}{c} 6.7 \pm 1.2^{b} \\ 25.4 \pm 1.4 \end{array}$

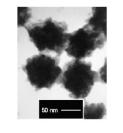
a Zeta potentials of the nanoparticle suspension in deionized distilled water were measured using the Brookhaven's Zeta PALS instrument.

^b Mean \pm S.D (n = 8)



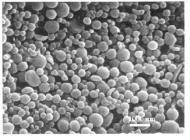


tion of FITC-conjugated glycol-chi (FTC-GC) nanoaggregates for 8 days after i.v. injection in tumor bearing rats at a dose of 10 mg/kg. Tissue accumulation measures Surface morphology data



Preparation

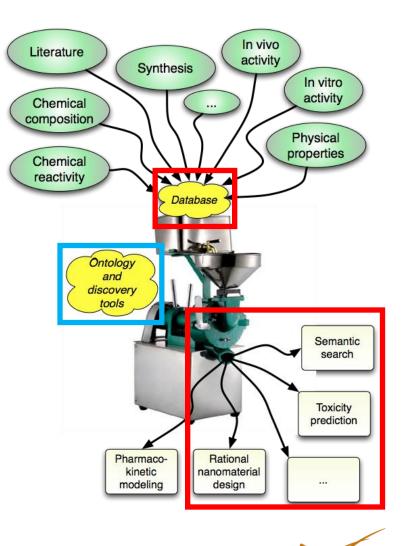
Chemical composition of nanoparticle formulation



Source: Chawla JS et al, Int J Pharm, 249, 127-38 (2002), Son YJ et al, J Control Release, 91, 135-145 (2003)

Nanomedicine community needs and response

- The nanomedicine community has an immediate need for nanomaterial informatics:
 - Understand nanomaterial toxicity and other biological properties
 - Search for existing data on nanoparticle synthesis and properties
 - Design nanoparticles, and other materials with custom properties for specific biological applications
- The community has responded with resources <u>including</u>
 - caBIG[®] Nanotechnology Working Group (<u>http://goo.gl/mi2D</u>)
 - NanoParticle Ontology (<u>http://www.nano-ontology.org/</u>)
 - caNanoLab (<u>http://goo.gl/XkBt</u>)
 - nano-TAB (<u>http://goo.gl/Wozi</u>)



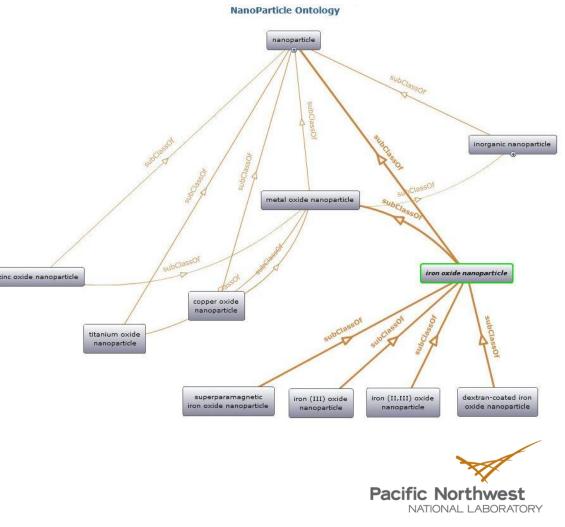
Proudly Operated by Battelle Since 1965

Pacific Northwest

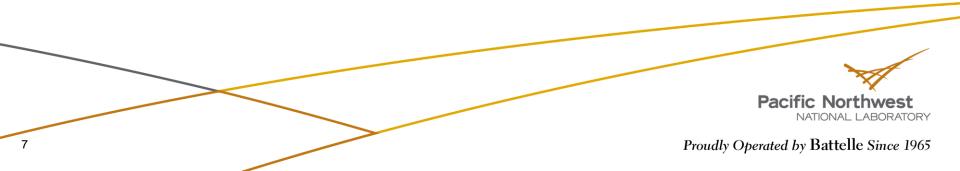
NATIONAL LABORATORY

The need for nanomedicine vocabularies and ontologies

- Standard terminology
 - Interdisciplinary discourse
 - Data sharing
 - Semantic interoperability
- Logical relationships between concepts
 - Data and knowledge management
 - Semantic search
 - Inference and association
- Classifiers for computer-aided materials design

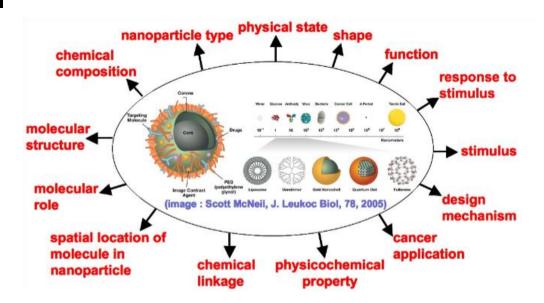


- Introduction to vocabulary in nanoinformatics
- NanoParticle Ontology design
- NanoParticle Ontology applications
- Future growth and development



NanoParticle Ontology (NPO) initial scope

- Capture knowledge underlying nanomaterial
 - Preparation
 - Chemical composition
 - Physiochemical characterization
 - Biological function/behavior
- Initial focus on cancer diagnosis and therapy
- Current growth to include a broader range of nanotechnology concepts





Thomas DG, Pappu RV, <u>Baker NA</u>. NanoParticle Ontology for Cancer Nanotechnology Research. *J Biomed Inform*, in press. doi:<u>10.1016/j.jbi.2010.03.001</u>

NPO initial goals

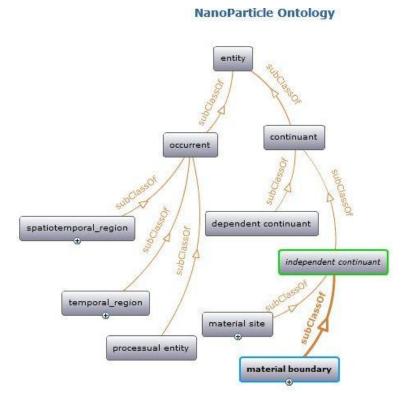
- 1. To provide terms for *annotating data* generated from research in cancer nanotechnology.
- 2. To provide the *knowledge framework* required for developing data sharing models and standards in nanomedicine.
- 3. To enable *semantic integration* of the data by providing the terms and relationships for data annotation.
- 4. To enable *unambiguous interpretation* of data pertaining to the description and characterization of nanomaterials.
- 5. To enable *knowledge-based searching* of the data for accessing and retrieving relevant information that facilitates *comparison of nanomaterials* and characterization results, leading towards knowledge enhancement and discovery.



NPO design principles

- Follows Basic Formal Ontology (BFO) design principles:
 - Provides a formal structure for classification of terms
 - Provides a set of well-defined principles known for best ontology practices in the biomedical arena
 - Helps make the NPO interoperable with other ontologies that have the formal structure of BFO
 - Information represented in the ontology will remain clear, rigorous and unambiguous
- Provides clear development/expansion path

Thomas DG, Pappu RV, <u>Baker NA</u>. NanoParticle Ontology for Cancer Nanotechnology Research. *J Biomed Inform*, in press. doi:<u>10.1016/j.jbi.2010.03.001</u>



NCBO BioPortal visualization of toplevel structure: <u>http://goo.gl/Wuxt</u>



NPO example classes

e.g., magnetic, pH-sensitive, hydrophilic, size, biodegradable, solid state, pharmacokinetic property, etc.

e.g., anticancer drug, targeting agent, spacer, image contrast agent, surface modifying agent, etc.

e.g., scanning electron microscope, atomic force microscope, etc.

e.g., nanoparticle, iron oxide nanoparticle, quantum dot, biodegradable nanoparticle, nanocage, nanotube, nanocantilever, nanosensor, carbon nanofiber, etc.

e.g., solid, liquid, emulsion, hydrogel, etc.

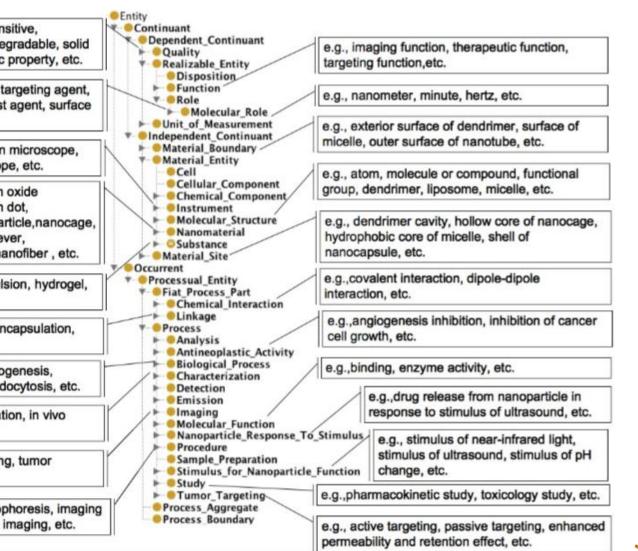
e.g., amide linkage, encapsulation, entrapment, etc.

e.g., metastasis, angiogenesis, receptor-mediated endocytosis, etc.

e.g., size characterization, in vivo characterization, etc.

e.g., diagnostic imaging, tumor imaging, etc.

e.g.,assay, gel electrophoresis, imaging technique, ultrasound imaging, etc.

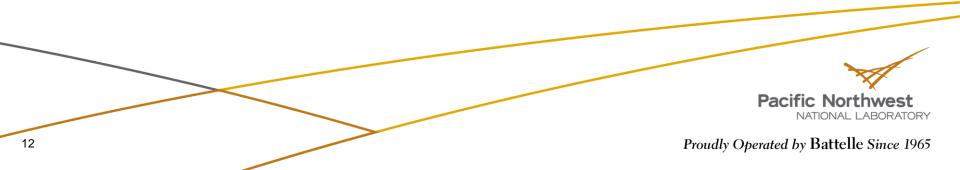




Pacific Northwest NATIONAL LABORATORY

Introduction to vocabulary in nanoinformatics

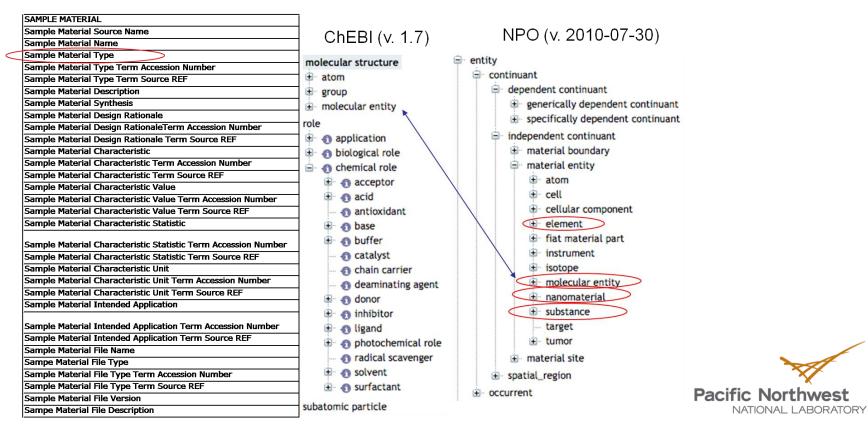
- NanoParticle Ontology design
- NanoParticle Ontology applications
- Future growth and development



Using the NPO for sharing nanotechnology data

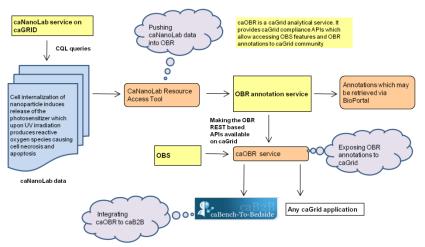
caNanoLab and nano-TAB

- Object structure
- Concept definitions
- Defined types and allowable values
- Semantic interoperability in data exchange



Using the NPO for searching biomedical and nanotechnology databases

- Collaboration with the National Center for Biomedical Ontology Uses the NPO and other ontologies for <u>semantic</u> search
- NCBO BioPortal indexes several major biomedical resources, including caNanoLab



BioPortal Resource Search View Demo!	
	Search
Ontology filters	Clear
1155 ARRS GoldMiner	1172881 🞼 Adverse Event Reporting Syst
15190 🕂 ArrayExpress	1630 Biositemaps
96338 ClinicalTrials.gov	40733 🗰 Conserved Domain Database
246 Jatabase of Genotypes and Phenotypes	
21272 Gene Expression Omnibus DataSets	10 823 MICAD
21140 Online Mendelian Inheritance in Man	923 Pathway Commons
832 MarmGKB [Disease]	1634 🗮 PharmGKB [Drug]
988 🗯 PharmGKB [Gene]	🕜 110241 🇤 PubChem
2000 Reactome	1033651 ResearchCrossroads
18581 Stanford Microarray Database	18324 UniProt KB
1477 🧟 WikiPathways	(2) 800 caNanoLab

	Property or Attribute from: NCI Thesaurus	Qualifier value from: SNOMED Clinical Terms						
uthor: investi	Cell from: BIRNLex	molecular structure from: Chemical entities of biological interest						
how deta	Murine Cell Types from: NCI Thesaurus	Cell Device Component from: NCI Thesaurus						
	Cellular Telephone from: NCI Thesaurus	Conceptual Entity from: NCI Thesaurus						
3nici 📕	Qualifier from: NCI Thesaurus	molecular entity from: Chemical entities of biological intere						
	THE from: Rat Strain Ontology	General Qualifier from: NCI Thesaurus						
thor:	Left from: Foundational Model of Anatomy	inbred strain from: Rat Strain Ontology						
investi	Index Medicus Descriptor from: Medical Subject Headings	Alphanumeric from: SNOMED Clinical Terms						
ow deta	cellular phenotype from: Mammalian phenotype	rat strain from: Rat Strain Ontology						
	Activity from: NCI Thesaurus	MeSH Descriptors from: Medical Subject Headings						
tinis	outer chorionic cell from: Mosquito gross anatomy	Descriptor from: SNOMED Clinical Terms						
ithor:	float ridge from: Mosquito gross anatomy	homoatomic molecular entity from: Chemical entities of biological interest						
investi	monoatomic entity from: Chemical entities of biological interest	Unit by Category from: NCI Thesaurus						
ow deta	functional entity from: Systems Biology	Geographic Area from: NCI Thesaurus						

Learn More About The Resources

Pacific Northwest NATIONAL LABORATORY

NCBO BioPortal: http://bioportal.bioontology.org/

Using the NPO for classification and modeling

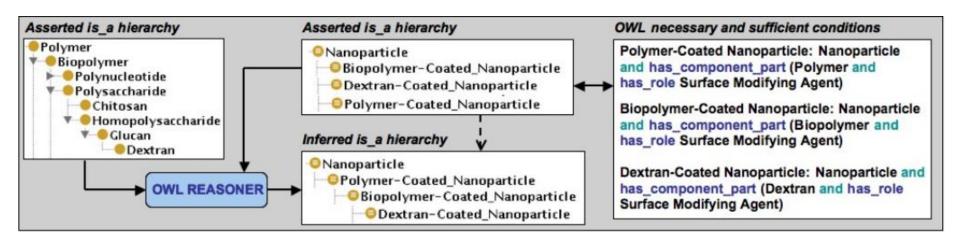
- SAR-based approaches
 - Machine learning for best descriptors
 - Simple regression and regression tree approaches
 - Ontology-based categorization and inference
- Embryonic zebrafish models
- Gold nanoparticles
- Collaboration
 - Stacey Harper, ONAMI
 - Kilian Weinberger and Eddie Zhang, WUStL

		Feature importance in predicting targets														
surface N	I,N,N 0	C	b	0.1	0.1	0.1	0.7	0.1	0.1	0.1	1	0.1	0.1	0.1	0.1	0.1
surface	2-2 0	C	0	0	0	0	0	0	0	0	0	0	0	0	0	0 -
surfa	ace 2 - O	0	D	0	0	0	0	0	0	0	0	0	0	0	0	0 -
surface 2-	-2-2 0	C	D	0	0	0	0	0	0	0	0	0	0	0	0	0 -
ch	arge 0	C	D	0	0	0	0	0	0	0	0	0	0	0	0	0 -
primary particle	size O	(D	1	0.6	0.5	1	1	0.5	0.7	1.1	0.6	0.7	0.6	0.5	0.4
concentration of TMA	ато.в <mark>20</mark>	.5	15.6	16.6	13.3	12.3	9.7	13.1	11.4	15.4	9.5	13.9	15.4	14.8	11.7	9.9 -
concentration of TMA	AT1.5 20.	.7 2	21.5						8.5			10.2		10.9		14.3
concentration of TM/	at10 <mark>- 13</mark>		9.9													10.7
concentration of ME	E0.8 - 12		9.2	6.9	7.7	7.1	5.5	6.4	6.4	8.9		17.3	8.9	8.4	6.4	11.3
concentration of ME	E1.5 5.8	3 1		10.8	7.7		5.8	8.9			7.3	8.1		8.6	7.8	5.7
concentration of ME	S0.8 - 6.2	2 1	10.5	7.5	4.3	8.3		16.2	3.7		6.7	9.7			8.1	25.1
concentration of ME	S1.5 <mark>- 18</mark>	.9 1	14.3	15.3	17.6	20.2	20.2		14.9	20.3	9.9	18.4	20.3	19.4	15.3	13.6
concentration of MEE	E0.8 0		8.9	0	8.2	7.3		6.2	14.5	0	11.3	0	0	0	6.9	0
concentration of MEE	E1.5 2.7	(C	7.1	8.6	3.4	6.4	6.6	15	4.2	12.2	3.8	4.2	4.1	7.1	6.7 -
size of T	тмат 0	(D	5.9	2.8	2.7	5.3	5.1	2.2	3.4	4.3	3	3.4	3.2	2.5	2.1
size of I	MEE 0	(D	0	0	0	0	0	0	0	0	0	0	0	0	0 -
size of I	MES - 0	C	D	0	0	0	0	0	0	0	0	0	0	0	0	0 -
size of M	EEE 0.1	(0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
	mort.yes	.24 dev.pro	g.yes.24	mort.yes	axis.yes	eye.yes	snout.yes	jaw.yes	otic.yes	notochord.yes	heart.yes	brain.yes	somite.yes p	ectoralfin.yes	trunkfin.yes	trunk.yes

Targets



Using the NPO for inference



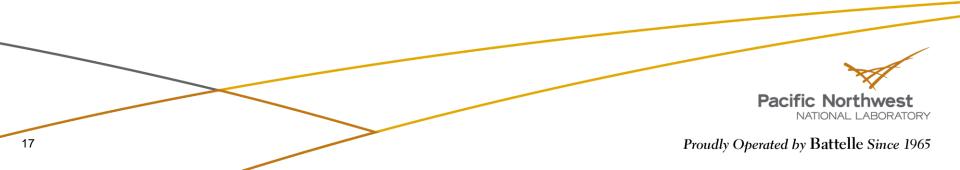
Why?

- Searching
- Model generalization and interpretability
- Linking observations
- How?
 - Ontology structure
 - Pellet reasoner

Example shows how an OWL reasoner infers parent-child relationships among *Polymer-Coated Nanoparticle*, *Biopolymer-Coated Nanoparticle*, and *Dextran-Coated Nanoparticle* based on their asserted Associations to and based on the asserted hierarchy of *Polymer*, *Biopolymer*, and *Dextran* respectively.

> Pacific Northwest NATIONAL LABORATORY

- Introduction to vocabulary in nanoinformatics
- NanoParticle Ontology design
- NanoParticle Ontology applications
- Future growth and development



NPO is a community project

- Governed and developed by the caBIG® Nanotechnology Working Group (<u>http://goo.gl/mi2D</u>)
- Freely available through
 - NPO website: <u>http://www.nano-ontology.org/</u>
 - NCBO BioPortal: <u>http://purl.bioontology.org/ontology/NPO</u>
 - NCI Meta-Thesaurus: <u>http://ncimeta.nci.nih.gov/</u>
- Community involvement welcomed <u>and needed!</u>
 - New concepts and growth
 - Harmonization and mapping
 - Additional applications

Funding sources

- U54 CA119342
- U54 CA119367
- U54 HG004028
- NCI caBIG[®]

Further reading

Thomas DG, Pappu RV, <u>Baker NA</u>. NanoParticle Ontology for Cancer Nanotechnology Research. *J Biomed Inform*, in press doi:<u>10.1016/j.jbi.2010.03.001</u>

Collaborators

caBIG[®] ICR Workspace, Raul Cachau, Gilbert Fragoso, Elaine Freund, Marty Fritts, Sharon Gaheen, Liz Hahn-Dantona Stacey Harper, Mark Hoover, Fred Klaessig, Juli Klemm, Michal Lijowski, David Paik, Sue Pan, Rohit Pappu, Persistent Systems Ltd, Stan Shaw, Eddie Xu, Kilian Weinberger, Trish Whetzel

