SWANSIOC
Scientific Discourse Representation

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October 27, 2008
Scientific Discourse
Scientific Discourse Project Goals

Provide a Semantic Web platform for scientific discourse in biomedicine

• linked to
  – key concepts, entities and knowledge

• specified
  – by ontologies

• integrated with
  – existing software tools

• useful to
  – Web communities of working scientists.
Strategy

• Stepwise alignment of key ontologies
• Early wins in real applications
• Forward-looking pre-alignments
• Practical validation with scientific users
• Iterative development
Some parameters

- **Discourse categories**: research questions, scientific assertions or claims, hypotheses, comments and discussion, and evidence.
- **Biomedical categories**: genes, proteins, antibodies, animal models, laboratory protocols, biological processes, reagents, disease classifications, user-generated tags, and bibliographic references.
- **Driving Biological Project**: cross-application of discoveries, methods and reagents in stem cell, Alzheimer and Parkinson disease research.
- **Informatics use cases**: interoperability of web-based research communities with
  - (a) each other
  - (b) key biomedical ontologies
  - (c) algorithms for bibliographic annotation and text mining
  - (d) key resources.
Iteration #1: SWAN+SIOC

• SIOC
  – http://sioc-project.org
  – Represent activities and contributions of online communities
  – Integration with blogging, wiki and CMS software
  – Use of existing ontologies e.g. FOAF, SKOS, DC

• SWAN
  – http://swan.mindinformatics.org
  – Represents scientific discourse (hypotheses, claims, evidence, concepts, entities, citations)
  – Used to create the SWAN Alzheimer knowledge base
  – Active beta participation of 144 Alzheimer researchers
  – Ongoing integration into SCF Drupal toolkit
Submission request to W3C (W3C Team Comment)

Semantically-Interlinked Online Communities (SIOC) Ontology Submission Request to W3C

Submitted materials

We, W3C Members - Asemantics S.R.L., DERI Galway at the National University of Ireland, Galway, Ireland, German Research Center for Artificial Intelligence (DFKI) GmbH, Forschungszentrum Informatik (FZI), Fraunhofer Gesellschaft, Fundación CTIC (Centro Tecnológico para el Desarrollo en Asturias de las Tecnologías de la Información y la Comunicación), OpenLink Software Inc., Opera Software, STFC (Science & Technology Facilities Council), Universidad Politécnica de Madrid, Department of Information and Communication Technology - University of Trento - hereby submit to the Consortium the following specification, comprising the following documents attached hereto:

1. SIOC Core Ontology Specification
2. SIOC Ontology: Applications and Implementation Status
3. SIOC Ontology: Related Ontologies and RDF Vocabularies
4. Snapshots of Namespace Documents in RDFS/OWL (ZIP Archive):
   ○ SIOC Core Ontology Namespace [ns.rdf]
   ○ SIOC Types Ontology Module Namespace [types.rdf]
   ○ SIOC Services Ontology Module Namespace [services.rdf]

which is referred to as "the Submission". We request the Submission be known as the SIOC Ontology Submission.
Social Semantic Information Spaces

Collaboration and Communication Tools
Blogs, Forums, OSNs, Wikis

Social Connectivity

World Wide Web
URIs, HTML, HTTP

Syntax

Web Semantics
RDFS, OWL, SPARQL, microformats

Semantic

Bringing the Web to its full potential

Digital Enterprise Research Institute
www.deri.ie
Blogosphere

Virtual Forum

Distributed Conversation

Unified Community

Usenetverse

One Person = Many User Accounts

Blogscape

Bulletin Board

Post

Post

Post

Post

Post

Post

Post

Post

Post

Shared Topic

Mailing List

Post

Post

Post

Post

Post

Post

Post

Listspace
The SIOC food chain

**Producers**
- Add-Ons and Fns for Exporting SIOC from Existing Apps
- SIOC from Semi-Structured Data or Queryable APIs
- Applications with Native Storage of SIOC Data
- Bypassing Apps by Directly Mapping RDBMS to SIOC

**Collectors**
- SIOC Crawlers and Aggregate Storage of Data
- Indexers of SIOC Instances w/o Full Storage

**Consumers**
- RDF Browsers and Other Custom SIOC Explorers
- SIOC Detectors and Clipping Applications
- Reuse and Import for Data Portability Requirements
- Graphical Vis of Derived SIOC Networks

**Food Chain of Applications**
The SIOC Ontology

- **Space**
  - has_space
  - subClassOf
  - has_parent

- **Site**
  - has_parent
  - has_host
  - has_scope

- **Role**
  - has_function
  - has_member

- **User**
  - has_member
  - has_creator

- **Container**
  - has_container
  - subClassOf

- **Item**
  - has_container
  - subClassOf

- **Forum**
  - has_container
  - subClassOf

- **Post**
  - topic
  - has_reply
  - has_creator
  - Tag / Category
SIOC types

- Social Media Contributions involve different types of content
  - Text, pictures, videos, reviews ...
  - Must be modeled in a different way
- SIOC Types module
  - http://rdfs.org/sioc/types
  - Defining several classes for specific Container and Item
    - Using rdfs:subClassOf, can be used by reasoners
  - Aligned with existing ontologies
    - DCMI ...
SIOC and friends

SIOC

SKOS

DC

Enabling networked knowledge.
SIOC data example

```xml
  <dcterms:title>Creating connections between discussion clouds with SIOC</dcterms:title>
  <dcterms:created>2006-09-07T09:33:30Z</dcterms:created>
  <sioc:has_container rdf:resource="http://johnbreslin.com/blog/index.php?sioc_type=site#weblog"/>
  <sioc:has_creator>
      <rdfs:seeAlso rdf:resource="http://johnbreslin.com/blog/index.php?sioc_type=user&amp;sioc_id=1"/>
    </sioc:User>
  </sioc:has_creator>
  <sioc:content>SIOC provides a unified vocabulary for content and interaction description: a semantic layer that can co</sioc:content>
  <sioc:has_reply>
  </sioc:has_reply>
</sioc:Post>
```
Semantics for data portability
Producing SIOC data

- Over 20 applications for producing SIOC data:
  - Many are free and open source
  - Blogs and forums: WordPress, phpBB, Drupal, b2evolution
  - “Legacy” applications: Mailing lists, IRC
  - New media: Twitter, Jaiku, Facebook, Flickr

- APIs for those who may wish to make their own producers:
  - PHP, Perl, Java, Ruby on Rails
SIOC applications
SIOC applications
The SWAN Project

- A **formal ontology** to record and present scientific discourse.
- A **knowledgebase** of hypotheses, claims, evidence, genes and proteins in Alzheimer’s Disease research.
- A **community** process built upon Alzforum.
- A **discovery tool** for conflicts, gaps, and missing evidence.
- An **information bridge** to promote collaboration.
Ontology

- [http://purl.org/swan/1.1/](http://purl.org/swan/1.1/)
- Version 1.2 with SIOC integration nearly complete.

Alzheimer Knowledge Base

- In Public Beta with 144 Alzheimer researchers actively participating.
- Leading Alzheimer researchers & institutes involved - including groups at three pharmaceutical companies.
- Hosted on Alzforum, > 5,000 registered members.
Welcome to the SWAN Alzheimer Knowledge Base

SWAN is the participatory knowledge base of Alzheimer Disease that YOU can help develop. SWAN is all about how you interpret, debate, ask questions and advance the science.

» Featured Contributions

» Hot Topics (browse all hypotheses)
- Amyloid Hypothesis of Alzheimer Disease (AD)
- Soluble oligomeric aggregates of Aβ are toxic to neurons and cause AD pathology
- Insoluble fibrillar Aβ leads to AD
- Defective mechanisms of Aβ clearance contribute to AD
- ApoE contributes to AD through multiple mechanisms
- Changes in calcium homeostasis may provide a common pathway for the neuropathological changes in AD
- Changes in presenilin function lead to dementia and neurodegeneration in Alzheimer Disease
- Misfolded proteins accumulated into protein aggregates characterizes the pathologic lesions of AD
- The molecular mechanisms of neuronal cell death are involved in the dysfunction and death of neurons in AD
- Synaptic loss appears to be the most powerful and ubiquitous proximate factor leading to the dementia of AD
- Failure of axonal transport might be the underlying basis for neurodegeneration in AD
- Cell membrane properties play a key role in AD Pathophysiology

» Mechanisms
- Energetics
- Functional Changes of Proteins
- Structural Changes of Proteins

» How to Contribute
- Build a hypothesis
- Critique a hypothesis
- Nominate a key paper
- Help find connections
- Propose new features
- Add supporting evidence

Contact us!

» Knowledge Base

Statements
1323 Research Statements
- 119 Hypotheses
- 21 with Extended annotation
- 98 with Simple annotation
- 1204 Claims

32 Research Questions
26 Comments

Publications
1036 Journal Articles
6 Journal Comments
2 Journal News
30 Web Comments

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Massachusetts General Hospital & Alzheimer Research Forum
Created by the SWAN Development Team
Give us your feedback!
Contributions from leading researchers
Contributions from leading researchers

Key research topics

- Amyloid Hypothesis of Alzheimer Disease (AD)
- Soluble oligomeric aggregates of Aβ are toxic to neurons and cause AD pathology
- Insoluble fibrillar Aβ leads to AD
- Defective mechanisms of Aβ clearance contribute to AD
- ApoE contributes to both through cholesterol acetate
- Changes in calcium homeostasis may provide a common pathway for the neuropathological changes in AD
- Changes in presenilin function lead to dementia and neurodegeneration in Alzheimer Disease
- Misfolded proteins accumulated into protein aggregates characterizes the pathologic lesions of AD
- The molecular mechanisms of neuronal cell death are involved in the dysfunction and death of neurons in AD
- Synaptic loss appears to be the most powerful and ubiquitous proximate factor leading to the dementia of AD
- Failure of axonal transport might be the underlying basis for neurodegeneration in AD
- Cell membrane properties play a key role in AD Pathology....
Contributions from leading researchers

Key research topics

Mechanisms of disease
Contributions from leading researchers

Mechanisms of disease

Contribute content
120 Hypothesis

Extended Annotation (2)

1. The Amyloid Hypothesis of Alzheimer Disease.
   Hardy J, Selkoe D J [2002]
   Contains 55 statements: 21 with evidence, 1 without evidence, and a total of 106 citations
   Relationships with external statements: 21 consistent, 5 inconsistent, 1 discussed, 13 alternative to
   Genes-Proteins:
   (in Homo sapiens): Amyloid beta A4 protein, APP, Psen1, Psen2, Psen3, ApoE, APOE, Tau, Microtubule-associated protein tau

2. The Aβ hypothesis will lead to rationally-designed therapeutic strategies for the treatment or prevention of Alzheimer disease.
   De Strooper B [2005]
   Contains 45 statements: 26 with evidence, 19 without evidence, and a total of 44 citations
   Relationships with external statements: 10 consistent, 3 inconsistent, 1 alternative to
   Genes-Proteins:
   (in Homo sapiens): Amyloid beta A4 protein, ApoE, APOE, APP, Beta-secretase 1, BACE1, Microtubule-associated protein tau, PSEN1, PSEN2, PSEN3, Presenilin-1

Simple Annotation (1)

1. Amyloid Cascade Hypothesis: The neurodegeneration of Alzheimer Disease is caused by Aβ deposited into plaques in brain tissue.

ApoE contributes to Alzheimer Disease through multiple mechanisms (13)
Soluble oligomeric aggregates of AB are toxic to neurons and cause AD pathology (6)

Extended Annotation (4)

1. Naturally secreted oligomers of amyloid beta protein potently inhibit hippocampal long-term potentiation in vivo.
   - Contains 28 statements: 28 with evidence, 0 without evidence and a total of 62 citations
   - Relationships with external statements: 16 consistent, 2 inconsistent, 1 discussed
   - Genes-Proteins: [Homo sapiens]: APP, Amyloid beta A4 protein precursor, IDE, Insulin-degrading enzyme, Presenilin-1

2. Oligomeric amyloid beta ligands (ADDLs) are a molecular basis for reversible memory loss.
   - Gong Yueson, Chang Lei, Lambert Mary P, Klein W L, Lacor Pascale N, Finch Caleb E, Krafft Grant A, and Viola Kirsten L [2003]
   - Contains 46 statements: 46 with evidence, 0 without evidence and a total of 106 citations
   - Relationships with external statements: 15 consistent, 4 inconsistent
   - Genes-Proteins: [Homo sapiens]: Proto-oncogene tyrosine-protein kinase Fyn

3. Oligomerization of Aβ 40 and 42 occurs via distinct pathways.
   - Contains 42 statements: 30 with evidence, 12 without evidence and a total of 52 citations
   - Relationships with external statements: 26 consistent, 2 inconsistent
Scientist view: toxic protein fragments believed responsible for AD.

Key information, gaps and conflicts.
Soluble oligomeric aggregates of AB are toxic to neurons and cause AD pathology (6)

Extended Annotation (4)

1. Naturally secreted oligomers of amyloid beta protein potently inhibit hippocampal long-term potentiation in vivo.
   Contains 28 statements: ![28 with evidence](28 with evidence) ![0 without evidence](0 without evidence) and a total of ![62 citations](62 citations)
   Relationships with external statements: ![16 consistent](16 consistent) ![2 inconsistent](2 inconsistent) ![1 discussed](1 discussed)
   Genes-Proteins: ![Homo sapiens](Homo sapiens): APP, Amyloid beta A4 protein precursor, IDE, Insulin-degrading enzyme, Presenilin-1

2. Oligomeric amyloid beta ligands (ADDLs) are a molecular basis for reversible memory loss.
   Gong Yueson - Chang Lei, Lambert Mary P, Klein W L, Lacor Pascale N, Finch Caleb E, Krafft Grant A, and Viola Kirsten L [2003]
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3. Oligomerization of Aβ 40 and 42 occurs via distinct pathways.
   Contains 42 statements: ![30 with evidence](30 with evidence) ![12 without evidence](12 without evidence) and a total of ![52 citations](52 citations)
   Relationships with external statements: ![26 consistent](26 consistent) ![2 inconsistent](2 inconsistent)
For any statement about AD, what is the evidence?

8. The amyloid cascade hypothesis has been modified to include soluble Aβ oligomers. Supporting(3)

9. Aβ oligomers are undetected in typical pathology assays, and thus constitute missing links in the pathogenic cascade. Supporting(1)

10. Aβ oligomers applied to brain slices or injected in vivo cause failure of hippocampal LTP. Supporting(4)

Supporting Evidence


11. Soluble Aβ oligomers have been implicated in physical degeneration of synapses. Support(2)

12. Soluble Aβ oligomers have been implicated in age-dependent onset of memory failure in APP transgenic mice. Supporting(4)

13. Memory failure in APP transgenic mice is reversed by anti-Aβ antibodies, and the memory recovery is rapid, occurring within 24 h of a single injection of antibody, without reducing amyloid plaque load. Supporting(4)
For any statement about AD, what is the evidence?

10. **Supporting Evidence**

Soluble oligomers of beta amyloid (1-42) inhibit long-term potentiation but not long-term depression in rat dentate gyrus. *Brain research*. 2002 Jan 11;924(2):133-40


Walsh D, Klyubin I, Fadeeva J, Cullen W, Anwy R, Wolfe M, Rowan M, Selkoe D


11. **Supporting Evidence**

Soluble Aβ oligomers have been implicated in physical degeneration of synapses. *SHOW Info*  *SHOW 2 Citations*: Supporting(2)  *SHOW 1 Related statements*: Consistent(1)

12. **Supporting Evidence**

Soluble Aβ oligomers have been implicated in age-dependent onset of memory failure in APP transgenic mice. *SHOW Info*  *SHOW 4 Citations*: Supporting(4)  *SHOW 1 Related statements*: Consistent(1)

13. **Supporting Evidence**

Memory failure in APP transgenic mice is reversed by anti-Aβ; antibodies, and the memory recovery is rapid, occurring within 24 h of a single injection of antibody, without reducing amyloid plaque load. *SHOW Info*  *SHOW 4 Citations*: Supporting(4)
Are statements inconsistent?
Can an experiment resolve them?

4. Although there are no known mutations of tau in AD, tau mutations cause FTDP-17 (frontotemporal dementia with parkinsonism linked to chromosome 17) and are associated with the development of corticobasal degeneration, progressive supranuclear palsy, and Pick’s disease. **SHOW Info**  **SHOW 1 Citations:** ▶️ Supporting(1)  **SHOW 1 Related statements:** ▶️ Consistent(1)

5. Interference with microtubule-dependent axonal transport is one possible mechanism by which altered tau exerts neurotoxicity. **SHOW Info**  **SHOW 1 Related statements:** ▶️ Consistent(1)

6. High levels of htau40 (the longest human tau isoform) overexpression in neuroblastoma, primary cortical neurons, and retinal ganglion cells (RGCs) have been reported to block the trafficking of membranous organelles and neurofilaments, suggesting that rates of fast and slow transport are impaired. **SHOW Info**  **SHOW 1 Citations:** ▶️ Supporting(1)  **SHOW 2 Related statements:** ▶️ Consistent(1)  ▶️ Inconsistent(1)

**Consistent statements**
- Human wild-type tau (the longest form), expressed about threefold over endogenous levels, induces neural dysfunction in entorhinal cortex at old age (more than 20 months), accompanied by synapse loss and accumulation of hyperphosphorylated tau resulting in a memory deficit, while adult mice (>12 months old) are different from non-Tg. Takashima A

**Inconsistent statements**
- Whether or not axonal transport is impaired depends not only on expression levels, as our Tau-4R mice expressed only about twofold over endogenous mouse tau, and we did not observe aggregates of tau. Van Leuven F

7. By analyzing axonal transport in optic axons from two different lines of mice that either overexpress or lack tau, it was determined that rates of fast and slow transport are not significantly impaired by modulating tau expression. **SHOW Info**

8. Axonal transport is not necessarily dependent on the presence of tau and is not significantly inhibited by moderately elevated levels of tau. **SHOW Info**

9. Previous studies showed that brain tau is absent in tau knock-out mice and is overexpressed in 8c mice. **SHOW Info**  **SHOW 2 Citations:** ▶️ Supporting(2)
Are statements inconsistent? Can an experiment resolve them?

4. Although there are no known mutations of tau in AD, tau mutations cause FTDP-17 (frontotemporal dementia with parkinsonism linked to chromosome 17) and are associated with the development of corticobasal degeneration, progressive supranuclear palsy, and Pick's disease. 

5. Interference with microtubule-dependent axonal transport is one possible mechanism by which altered tau exerts neurotoxicity. 

6. High levels of htau40 (the longest human tau isoform) overexpression in neuroblastoma, primary cortical neurons, and retinal ganglion cells (RGCs) have been reported to block the trafficking of membranous organelles and neurofilaments, suggesting that rates of fast and slow transport are impaired.

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9. Previous studies showed that brain tau is absent in tau knock-out mice and is overexpressed in 8c mice.
Science Collaboration Framework

- SCF is a special distribution of Drupal
  - Designed to support biomedical web communities.
  - Collaboration of Harvard, Alzforum, MGH.
  - Initial focus communities: Stem Cells, Parkinson’s Disease
- SCF is being developed to work with SWAN ontology.
  - Drupal “Node proxy” architecture reads RDF triples.
  - Specific models for biomedical entities.
- Vision
  - Many SCF-based communities
  - Resource, information and discourse sharing via triple
Behind the Stem Cell Breakthrough


The stunning announcement by Japanese and American research teams that they have obtained highly promising stem cells without having to destroy an embryo could help free scientists from shackles that have long hobbled their efforts. It is especially important for a critical field of research that is far behind where it could have been if the Bush administration and Congressional conservatives had not thrown up so many roadblocks.

Commentaries

May 30, 2008
Genomic approaches provide insights into the molecular basis of pluripotency

more
Oxidative Stress Hypothesis

Morbus Parkinson [PD (Parkinson's disease)] is a neurodegenerative disorder affecting dopaminergic neurons in substantia nigra. Mitochondrial respiratory complex I deficiency and oxidative stress have been reported to occur in these neurons, and cytoplasmic aggregates ('Lewy bodies') of α-synuclein and other proteins have been observed in the affected neurons.

Autosomal recessive mutations within the Parkin gene are associated with degeneration of the substantia nigra and locus coeruleus and an inherited form of Parkinson's disease (PD). As loss-of-function mutations in parkin are responsible for familial variants of PD, conditions that affect wild-type parkin are likely to be associated with increased risk of idiopathic disease. Previous studies uncovered a unique vulnerability of the parkin protein to dopamine (DA)-induced aggregation and inactivation. In this study, we compared several proteins that share structural elements or ubiquilin activity with parkin. We report that oxidative stress in several cell lines and primary neurons induces the aggregation of parkin into high molecular weight species, at least a portion of which are self-associated homo-multimers.

While parkin was preferentially affected by excess DA, each of the E3 proteins tested were made more insoluble by oxidative stress, and they varied in degree of susceptibility (e.g. parkin > HRRP congruent with CHAP > p.Cbl > ERP4). These conditions of oxidative stress were also associated with decreased parkin E3 ligase activity. Similar to recently conducted studies on alphasynuclein processing, both macroautophagy and the proteasome participate in parkin degradation, with the proteasome playing the predominant role for normal parkin turnover and macroautophagy being more important in the degradation of aggregated parkin.

These data further highlight the selective vulnerability of parkin to DA-induced modifications, demonstrating for the first time the ability of both endogenous and ectopically expressed parkin to transition into an insoluble state in part through self-association and next page.

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REFERENCES


Commentary

Role of Prostaglandin E2 in stem cell development

Added: Wednesday, 22 August, 2007, 15:51 GMT 16:51 UK


John Doe, Director, BioBlah

Added: Wednesday, 22 August, 2007, 15:51 GMT 16:51 UK
SWAN-SIOC Integration

- SIOC OWL-DL compliance (Core + Types)
- New SIOC Type: OnlineJournal
- SWAN JournalArticle, Citation, DiscourseElement -> SIOC Item
- SWAN WebArticle, WebNews, WebComment -> SIOC Post
- SWAN discourse properties -> SIOC related_to
- SWAN “Tag” replaced by Tag Ontology + MOAT
- SWAN ResearchStatement linked by SIOC “EmbedsKnowledge” to SIOC Items
- Pre-aligning SWAN Citation with BIBO
Looking Ahead

• **SWAN 1.2** (Q4 2008)
  – will be aligned with SIOC

• **SWAN 1.3** (Q1 2009)
  – plans to align with Biblio
  – will model document-embedded metadata

• **SWAN+SIOC**
  – will be a joint member submission to W3C
SWAN+SIOC Team

DERI: Uldis Bojars, John Breslin*, Ronan Fox, Alexandre Passant, Mathias Samwald, Holger Stenzhorn
Eli Lilly & Company - Susie Stephens
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Jacobs University: Christophe Lange
Massachusetts General Hospital - Marco Ocana
Yale Medical School - Kei Cheung

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