### "Simple, ontology-based representation of biomedical statements through fine-granular entity tagging and new web standards"

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Started out doing experimental neuroscience then switched to Semantic Web / ontologies for biomedical, pharmaceutical, neuroscientific, cognitive... R&D





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### World Wide Web Consortium

### "Semantic Web for Health Care and Life **Science Interest Group"**







### Linking Open Data (LOD) cloud



### Query the Neurocommons Knowledge Base: Find candidate genes known to be involved in signal transduction and active in Pyramidal Neurons!

prefix go: <http://purl.org/obo/owl/GO#> prefix rdfs: <http://www.w3.org/2000/01/rdf-schema#> prefix owl: <http://www.w3.org/2002/07/owl#> prefix mesh: <http://purl.org/commons/record/mesh/> prefix sc: <http://purl.org/science/owl/sciencecommons/> Mesh: Pyramidal Neurons prefix ro: <http://www.obofoundry.org/ro/ro.owl#> select ?genename ?processname where { graph <http://purl.org/commons/hcls/pubmesh> ?paper ?p mesh:D017966 . 4 ?article sc:identified by pmid ?paper. Pubmed: Journal Articles ?gene sc:describes gene or gene product mentioned by ?article. graph <http://purl.org/commons/hcls/goa> { ?protein rdfs:subClassOf ?res. ?res owl:onProperty ro:has\_function. ?res.owl:someValuesFrom?res2 ?res2 owl:onProperty ro:realized\_as. ?res2 owl:someValuesFrom ?process. Entrez Gene: Genes graph <http://purl.org/commons/hcls/20070416/classrelations> {{?process <http://purl.org/obo/owl/obo#part\_of> go:GO\_0007166} union {?process rdfs:subClassOf go:GO 0007166 }} ?protein rdfs:subClassOf ?parent. ?parent owl:equivalentClass ?res3. ?res3 owl:hasValue ?gene. GO: Signal Transduction graph <http://purl.org/commons/hcls/gene> { ?gene rdfs:label ?genename } graph <http://purl.org/commons/hcls/20070416> { ?process rdfs:label ?processname}

Inference`required

(Figure by Alan Ruttenberg)

# Results

processname
arrestin mediated desensitization of G-protein coupled receptor protein signaling pathway
transmembrane receptor protein tyrosine kinase activation (dimerization)
adenylate cyclase activation
adenylate cyclase activation
negative regulation of adenylate cyclase activity
Notch receptor processing
negative regulation of Wnt receptor signaling pathway
G-protein coupled receptor protein signaling pathway
G-protein coupled receptor protein signaling pathway
G-protein coupled receptor protein signaling pathway
G-protein coupled receptor protein signaling pathway
G-protein coupled receptor protein signaling pathway
G-protein coupled receptor protein signaling pathway
G-protein coupled receptor protein signaling pathway
transmembrane receptor protein tyrosine kinase signaling pathway
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transmembrane receptor protein tyrosine kinase signaling pathway

prefix go: <http://purl.org/obo/owl/GO#> prefix rdfs: <http://www.w3.org/2000/01/rdf-schema#>

prefix owl: <http://www.w3.or prefix mesh: <http://purl.or mons/record/me s/> prefix sc: <http://purl.org/s ce/owl/sciencecom ramida Mesh Neu ons prefix ro: <http://www.ob dry.org/ro/ro.owl#> select ?genename ?proc ame where { graph <http://purl.org/co</pre> ns/hcls/ iesh> ?paper ?p mesh:D017 ?article sc:identified by print-Pubmed: Journal Articles ?gene sc:describes\_gene\_or\_gene\_product\_mentioned\_by ?article. graph <http://purl.org/commons/hcls/goa> { ?protein rdfs:subClassOf ?res. ?res owl:onProperty ro:has function. ?res owl:someValuesFrom ?res2. ?res2 owl:onProperty ro:realized as. ?res2 owl:someValuesFrom ?process. Entrez Gene: Genes graph <http://purl.org/commons/hcls/20070416/classrelations> {{?process <http://purl.org/obo/owl/obo#part\_of> go:GO\_0007166} union {?process rdfs:subClassOf go:GO 0007166 }} ?protein rdfs:subClassOf ?parent. ?parent owl:equivalentClass ?res3. ?res3 owl:hasValue ?gene. GO: Signal Transduction graph <http://purl.org/commons/hcls/gene> { ?gene rdfs:label ?genename } graph <http://purl.org/commons/hcls/20070416> { ?process rdfs:label ?processname}

Inference`required



### but





# still very few tools suitable for end-users. (researchers, clinicians, anyone)





# Hypothesis!

many relevant problems could be solved with less complicated solutions.

and less complicated solutions could work better in practice.





### let's test this hypothesis.

# build a simple system, and try to do, well, everything with it.

tagging, converting data, publishing, searching, aggregating...

at the very least, i will end up with a system that i can actually use for my projects...





### 'associative tags'







### tagging statements, not documents. tagging with entities, not strings.







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	Generator				
	aTags ("associative tags") are snippets of HTML that capture the information that is most important to you in a machine-readable, interlinked format, making it easier for you and others to see the big picture.				
	aTag Generator Bookmarklet				
	With this bookmarklet you can create aTags for any kind of content on the web. To use it:				
	<ul> <li>Drag the aTag this bookmarklet to your bookmarks bar. (You might need to enable the bookmarks bar in your browser first.)</li> <li>When you are at a webpage that contains a snippet of text that you want to capture with an aTag, select the snippet of text, then click on the aTag bookmarklet in your bookmarks bar.</li> <li>A pop-up window will appear, containing the snippet of text you selected. Add tags to this snippet of text by typing in the box below it. Matching terms will be suggested as you type. Tag recommendation is currently based on DBpedia. If no suitable term already exists, you can choose to create a new term.</li> <li>When you are finished, click on 'Generate aTag'.</li> <li>You can copy and paste the generated aTag into your HTML-based application (such as a Wordpress blog, content management system, e-mail). The aTags on the web will be found by RDF-enabled search engines.</li> <li>If you are an RDF/OWL enthusiast, you can also visualize the RDF in the aTag you created with the RDFa highlight bookmarklet you can find here.</li> </ul>				
-	Technical Background				
East	aTags are based on Semantic Web standards and Linked Data practices. Specifically, they make use of RDFa, the SIOC vocabulary and	~			
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Huperzine A, a nootropic alkaloid, inhibits N-methy dissociated hippocampal neurons.	r	111
NMDA channel		
Zhang JM, Hu GY. NMDA receptor		
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one of the most promising agents to treat Alzheime	er 🔤	
found to inhibit the N-methyl-D-aspartate (NMDA) n addition to causing an inhibitory effect on acetylchc	ist)	
mechanisms underlying NMDA receptor inhibition we voltage-clamp recording in CA1 pyramidal neurons hippocampus. Huperzine A reversibly inhibited the I microM, Hill coefficient=0.92), whereas it had no eff amino-3-hydroxy-5-methyl-4-isoxazole propionate ( non-competitive, and showed neither 'voltage-dep(		
IC(50) values of huperzine A were neither altered t Fertig	Zotero 🛒	
(5 microM) and dithiothreitol (5 mM) to the external solution. However, addition	n of N-methyl-D-aspartate-induced current in rat di	
huperzine A concentration-response curve.From these we suggest that huper as a non-competitive antagonist of the NMDA receptors, via a competitive inter with one of the polyamine binding sites. The potential relevance of NMDA recep	zine A acts raction ptor	
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"Evodia rutaecarpa (Rutaceae) is used in TCM for cardiotonic, restorative and analgesic effects" aTags: Evodiamin (Source)	ie Analgesic Heart	
"Coptis chinensis (Ranunculaceae) has been used in TCM for several conditions. A methanol extract fraction jatrorrhizine and berberine are MAO inhibitors [Kong et al], indicating potential antidepressant activity, and C. chi alkaloids isolated from this plant (berberine, coptisine and palmatine) are reported to be anti-Cholinesterase" aTags Monoamine oxidase inhibitor Acetylcholinesterase inhibitor (Source)	of C. chinensis, inensis and some Coptis chinensis	
"In TCM, Codonopsis pilosula (Campanulaceae) root is used for various disorders including amnesia, and is beli blood circulation and enhance vitality" aTags: Codonopsis pilosula Therapy Amnesia Circulatory System (Source)	ieved to promote	
"Biota orientalis (Coniferae) is used in TCM for insomnia and amnesia" aTags: Biota orientalis Insomnia Amnesia (So	urce)	
"A crude alcoholic extract of Angelica archangelica (Umbelliferae), which has been used in TCM for cerebral dis nicotine binding to nicotine receptors in a concentration-dependent manner, but it is unknown if this effect was du antagonistic binding" aTags: Angelica Nicotinic acetylcholine receptor (Source)	seases, displaced ue to agonistic or	
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## there is more than meets the eye... **RDFa** + SIOC +domain ontologies/terminologies





## What the machine sees...

<http://hcls.deri.org/atag-data/pastebin.html#49ddfee65f7f4> a sioc:Item ;

sioc:content "Huperzine A acts as a non-competitive antagonist of the NMDA receptors"@en ; sioc:topic <http://dbpedia.org/resource/Huperzine\_A> , <http://purl.org/obo/owl/GO#GO\_0048019> , <http://dbpedia.org/resource/NMDA\_receptor> ; rdfs:seeAlso <http://www.ncbi.nlm.nih.gov/pubmed/11516831> .



## RDFa is simple to embed into existing systems websites, blogs, wikis, e-mails, biomedical databases...

handling data and annotations via Copy & Paste





### → We do not need to build everything from scratch





### Some aTags about neuropharmacology etc.

Below I have collected some interesting statements from research papers I recently stumbled upon. They are encoded as <u>aTags</u>.

| "Huperzine A acts as a non-competitive antagonist of the NMDA receptors" aTags: <u>Huperzine A receptor</u> <u>antagonist activity</u> <u>NMDA receptor</u> (<u>Source</u>) |

| "some effects of CDP-choline could be mediated by changes in brain platelet-activating factor (PAF) levels" aTags: <u>Citicoline</u> <u>Platelet-activating factor</u> (<u>Source</u>) |

| "Changes in brain striatum dopamine and acetylcholine receptors induced by chronic CDP-choline treatment of aging mice" aTags: <u>Striatum Dopamine receptor</u> <u>Acetylcholine receptor</u> <u>Citicoline</u> (<u>Source</u>) |

| "changes in ERK phosphorylation in hippocampus and PFC were regulated by GABAA receptor in a learning and memory paradigm under acute restraint stress conditions" aTags: <u>MAPK/ERK pathway Hippocampus</u> <u>Stress</u> (<u>Source</u>)|

| "our data suggest actions of memantine beyond NMDA receptor antagonism, including stimulating effects on cholinergic signalling via muscarinic receptors" aTags: <u>Memantine Muscarinic acetylcholine receptor</u> (<u>Source</u>)|

Written by admin March 18th, 2009 at 8:32 pm

Posted in Uncategorized

## add to blog post





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### SIDER drug side effect data

### 

This document/database contains information about side effects (adverse drug reactions) derived from <u>SIDER</u>. Relevant terms are mapped to DBpedia, the OBO Disease ontology and the OBO symptom ontology. Mappings were established via shared PubChem and UMLS identifiers. SIDER entries where no mapping for drug or disease/symptom could be established were omitted.

License: Except as otherwise noted, this work is licensed under a <u>Creative Commons Attribution-Noncommercial-Share Alike 3.0 License</u>. This data has been derived from a dataset by Kuhn et al. See <u>http://sideeffects.embl.de/download/</u> for further information (including information about commercial use).

Disclaimer: The content of this document/database is intended for educational and scientific research purposes only. It is not intended as a substitute for professional medical advice, diagnosis or treatment.

This document was generated by Matthias Samwald on 30 April 2009

```
| " <u>methadone</u> might cause <u>weight loss</u> . " |
```

| " <u>methadone</u> might cause <u>urinary retention</u> . " |

| " <u>methadone</u> might cause <u>palpitations</u> . " |

" <u>methadone</u> might cause <u>constipation</u> . " |

" <u>methadone</u> might cause <u>weakness</u> . " |

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" <u>methadone</u> might cause <u>cardiomyopathy</u> . "

## database converted to aTags

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### "Substance A interacts with receptor B in region C of the brain"

### "<u>Region C</u> has strong <u>axonal projections</u> into region D"

### "<u>Region D</u> is implicated in the processing of aversive stimuli"



# Standing on the shoulders of giants clouds







# Linked Data paradigm:

# Entities have URIs that can be resolved to yield further information







### Some aTags about neuropharmacology etc.

Below I have collected some interesting statements from research papers I recently stumbled upon. They are encoded as <u>aTags</u>.

| "Huperzine A acts as a non-competitive antagonist of the NMDA receptors" aTags: <u>Huperzine A receptor</u> antagonist activity <u>NMDA receptor</u> (<u>Source</u>) |

some effects of CDP-choline could be mediated by changes in brain platelet-activating factor (PAF) levels"

http://dbpedia.org/resource/Huperzine\_A

of aging mice" aTags: Striatum Dopamine receptor Acetylcholine receptor Citicoline (Source)

| "changes in ERK phosphorylation in hippocampus and PFC were regulated by GABAA receptor in a learning and memory paradigm under acute restraint stress conditions" aTags: <u>MAPK/ERK pathway Hippocampus Stress</u> (<u>Source</u>)|

| "our data suggest actions of memantine beyond NMDA receptor antagonism, including stimulating effects on cholinergic signalling via muscarinic receptors" aTags: <u>Memantine Muscarinic acetylcholine receptor</u> (<u>Source</u>)|

Written by admin March 18th, 2009 at 8:32 pm Posted in Uncategorized











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remove all (x) all_text_1:"huperzine" (x) is_atag:true	Huperzine A ameliorates the impaired memory naturally occurring or induced by scopolamine in aged rats
Search ( press ESC to close suggestions)	Huperzine A Protects Isolated Rat Brain Mitochondria against beta-Amyloid Peptide. Huperzine A Mitochondrial
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Mitochondrial NMDA receptor Non-competitive inhibition Scopolamine	Huperzine A is a novel promising acetylcholinesterase inhibitor. Huperzine A Acetylcholinesterase inhibitor
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aTag true	Huperzine A, a novel promising acetylcholinesterase inhibitor Huperzine A Acetylcholinesterase inhibitor
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# Developers need...

understandable and predictable data structures across distributed data sources

### ability to integrate into existing (web) applications, rather than building everything from scratch

simple means to develop GUIs to present and manipulate data





```
'simple'
                        . . .
               Free text
                                              . . .
         Free text + simple entity
         annotation
         Free text + relation annotation
                              Classical relational database
        . . .
        Simple ontology
             Fully formalized, exhaustive ontology
'complex'
```

Konrad Lorenz Institute for Evolution & Cognition Research



start simple, not complex

balance 'semantics' and 'pragmatics'

blur distinction between 'text' and 'data'

let real biomedical projects and user feedback drive developments





# Todo

convert more data

### curate more papers

# improve software (e.g., tag recommendation based on NCBO OBA etc.)

align with discourse ontologies (SWAN, SALT etc.)

learn from it



### creating aTags and aTagenabled applications is simple and fun!

### if you want to participate, contact me!



Tom Sawyer convincing someone else to do his work





### Early prototypes:

### http://hcls.deri.org/atag

Bye!



