Improving Text Mining with Controlled Natural Language: A Case Study for Protein Interactions

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DILS'06, Hinxton (UK)
21 July 2006

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Introduction

- Biomedical literature is growing at a tremendous pace
- *PubMed* contains 16 million articles and grows by over 600'000 articles per year
- Computational support is needed!

Today's Solution

The β-adaptin clathrin adaptor interacts with the mitotic checkpoint kinase BubR1

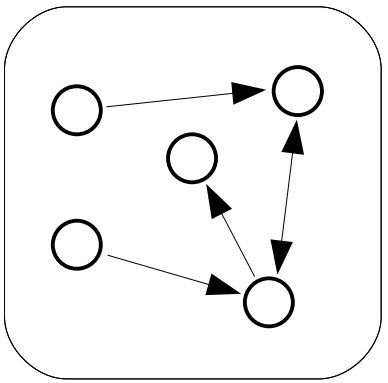
Corinne Cayrol, Céline Cougoule, Michel Wright

Abstract

The adaptor AP2 is a heterotetrameric complex that associates with clathrin and regulatory proteins to mediate rapid endocytosis from the plasma membrane. Here, we report the identification of the mitotic checkpoint kinase BubR1 as a novel binding partner of beta2-adaptin, one of the AP2 large subunits. Using two-hybrid experiments and in vitro binding assays, we show that beta2-adaptin binds to BubR1 through its amino-terminal beta2-'trunk' domain, while the beta2-binding region of BubR1 maps to the carboxy-terminal kinase domain. Subcellular immunolocalization studies suggest that the interaction between BubR1 and beta2-adaptin could take place in the cytosol at any time during the cell cycle. In addition, we found that BubR1 and the BubR1-related kinase, Bub1, also bind to beta-adaptins of other AP complexes. Together, these results support a model in which the mitotic checkpoint kinases BubR1 and BuB1, by binding to beta-adaptins, may play novel roles in the regulation of vesicular intracellular traffic.

Keywords: Protein interactions; Two-hybrid; Vesicular traffic; Adaptor protein; Protein kinase; Mitotic checkpoint.

NLP, manual annotation



Our Approach

- Let the researchers express their own results in a formal language
- Perfect processing of scientific results by computers
- This formal language has to be ...
  - easy to learn and understand
  - expressive enough to express even complicated scientific results

Knowledge Representation Languages

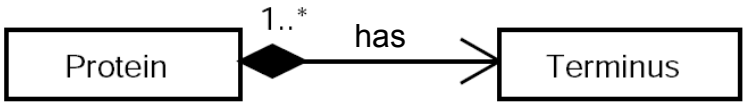
OWL with RDF/XML

```
<owl:Class rdf:ID="Protein">
  <rdfs:subClassOf>
    <owl:Restriction>
      <owl:onProperty rdf:resource="#has"/>
      <owl:someValuesFrom rdf:resource="#Terminus"/>
    </owl:Restriction>
  </rdfs:subClassOf>
</owl:Class>
```

ACE

Every protein has a terminus.

UML



Description Logics

$$Protein \sqsubseteq \exists has.Terminus$$

first-order logic

$$\forall X(protein(X) \rightarrow \exists Y(terminus(Y) \wedge has(X,Y)))$$

Attempto Controlled English (ACE)

- Formal language that looks like natural English
- Unambiguously translatable into first-order logic
- Restricted grammar
- Unlimited vocabulary
- `www.ifi.unizh.ch/attempto`

Formal Summaries

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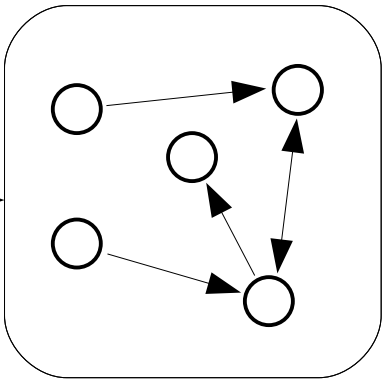
ACE Summary: Beta2-Adaptin binds BubR1 in Yeast-Two-Hybrid. A trunk-domain of Beta2-Adaptin interacts-with BubR1. Bub1 interacts-with the trunk-domain of Beta2-Adaptin. Bub1 interacts-with every beta-sheet of AP and BubR1 interacts-with every beta-sheet of AP.



Formal Summaries

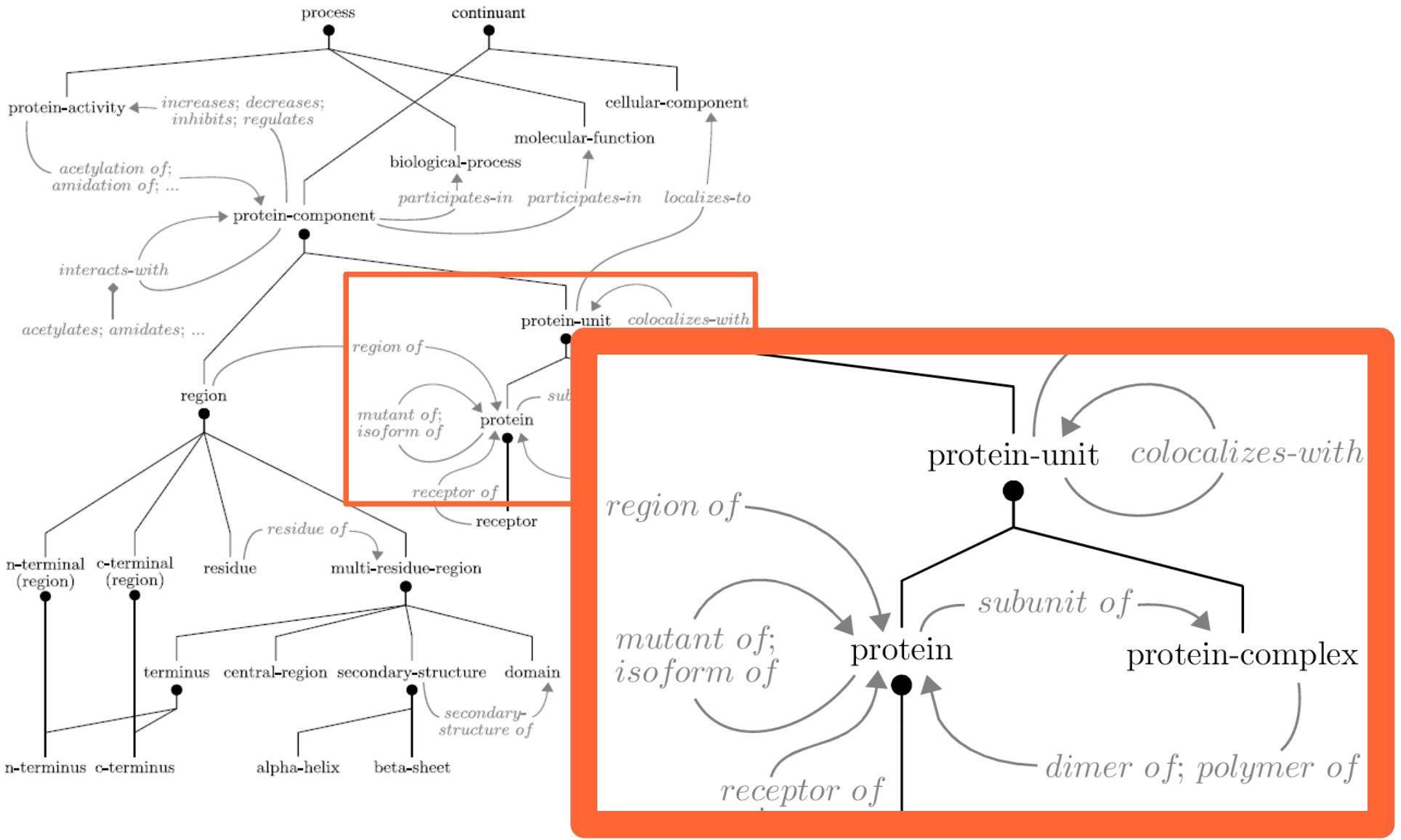
ACE text

BubR1 interacts-with a trunk-domain of Beta2-Adaptin.

Logical representation (DRS)

```
[A, B, C, D]
named(A, BubR1)-1
object(A, atomic, named_entity, object, cardinality, count_unit, eq, 1)-1
named(B, Beta2-Adaptin)-1
object(B, atomic, named_entity, object, cardinality, count_unit, eq, 1)-1
object(C, atomic, trunk-domain, unspecified, cardinality, count_unit, eq, 1)-1
relation(C, trunk-domain, of, B)-1
predicate(D, unspecified, interact_with, A, C)-1
```

Ontology for Protein Interactions

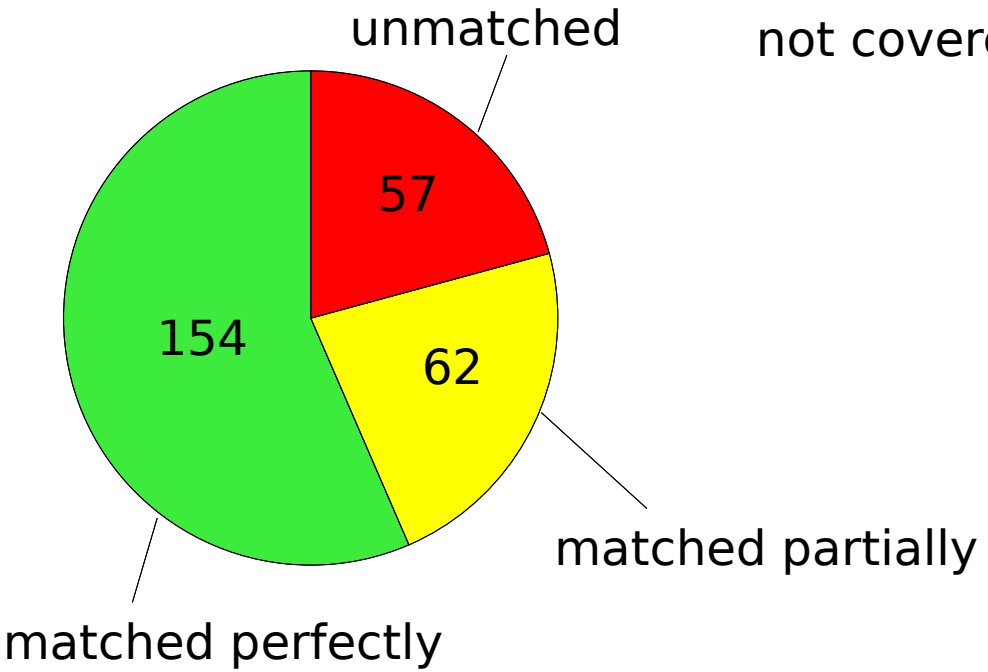


Empirical Study

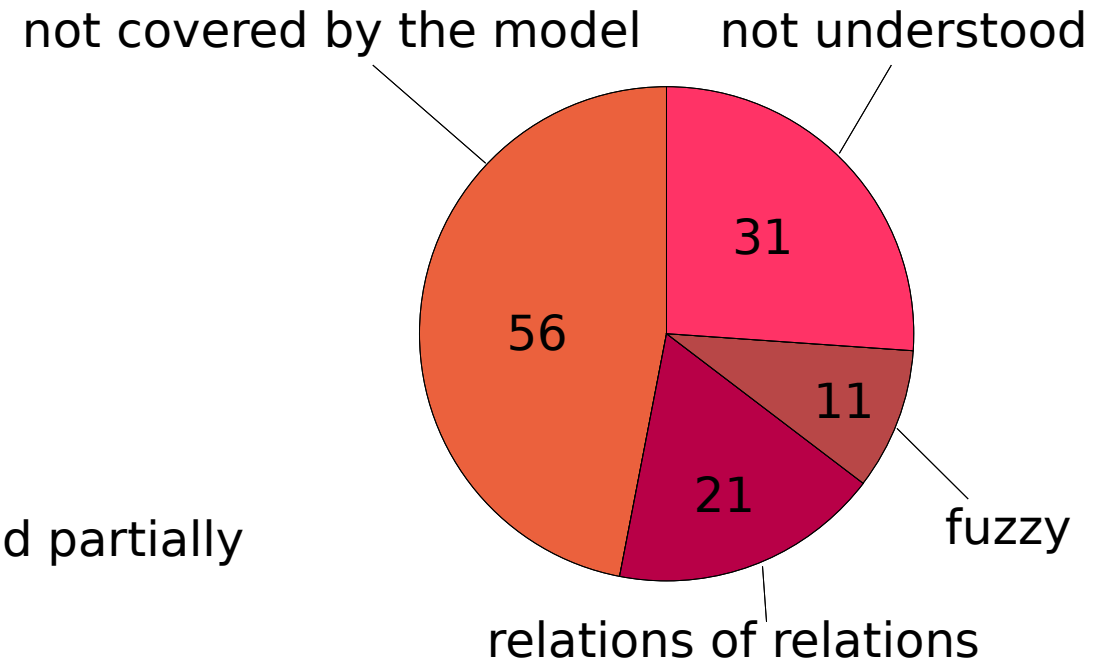
- "How suitable is ACE together with our ontology to express scientific results of protein interactions?"
- Manual translation of 273 facts about protein interactions
- These facts are subheadings of the "Results"-sections of 89 articles (journals by *Elsevier*)

Empirical Study

Total:



Non-perfect:

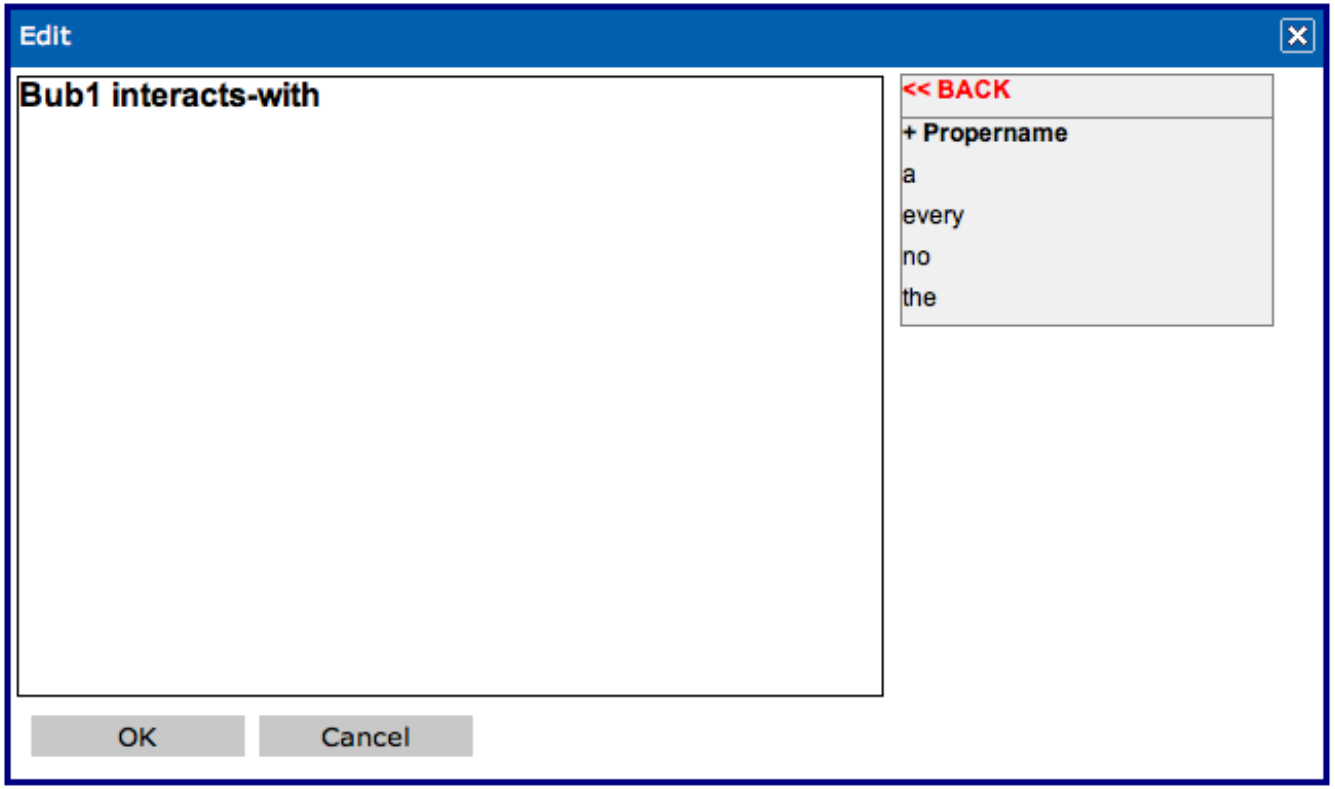


Authoring tool

- Helps writing ACE sentences
- Shows step by step the possible continuations of the sentence
- New words can be created on-the-fly
- Awareness of the underlying ontology
- The users do not need to know the details of the ACE syntax and of the underlying ontology

Authoring tool: Prototype demo

http://gopubmed.biotec.tu-dresden.de/AceWiki/



Benefits of our Approach

- Consistency / redundancy checks
  - “Is there a paper that contradicts my results?”
  - “Is there a paper that comes to the same or similar results?”
- Answer extraction
  - “Which proteins interact with a certain domain of protein X?”
- Automatically updated knowledge bases
  - “Give me an overview of the relations of a protein X to other proteins!”

Conclusions

- Formal summaries for scientific articles can make text mining easier and more powerful
- ACE combines the power of ontologies with the convenience of natural language
- Let the researchers formalize their own results!

Thank you for your attention!

Questions
&
Discussion

Subheadings: Example

2. Results

2.1. YETI binds specifically to both KHC and KLC in the yeast two-hybrid system

To identify proteins that may help kinesin perform its intracellular functions, yeast two hybrid screens were performed to identify *Drosophila* proteins that bind to the kinesin tail domain. Amino acids 675-975 of the kinesin heavy chain and the tetratricopeptide (TPR) motifs of the kinesin light chain were subcloned into the LexA DNA-binding domain plasmid pEG202 and used to screen the RELY1

Degree of Matching: Examples

- Matched perfectly:
  - *Interaction of Act1 with TRAF6*
  - → *Act1 interacts-with TRAF6.*
- Matched partially:
  - *The mtFabD protein is part of the core of the FAS-II complex*
  - → *MtFabD is a subunit of FAS-II.*
- Unmatched:
  - *Cav1 interacts differentially with distinct Dyn2 forms*

Reasons for Non-perfect Matching: Examples

- Not covered by the model:
  - *Daxx Potentiates Fas-Mediated Apoptosis*
- Relations of relations:
  - *Kal-GEF1 activation of Pak does not require GEF activity*
- Fuzzy:
  - *ANKRD1 contains potential CASQ2 binding sequences located in both its NT- and CT-regions*
- Not understood:
  - *hSrb7 does not interact with other nuclear receptors*