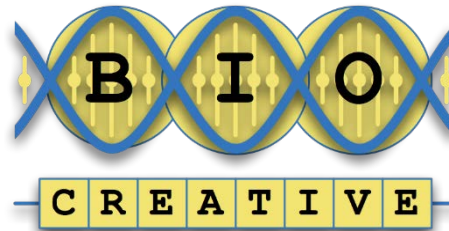


BioCreative Challenges

Information Retrieval and Text Mining for Biology

SIB

June 4, 2015.



Cecilia N. Arighi, PhD

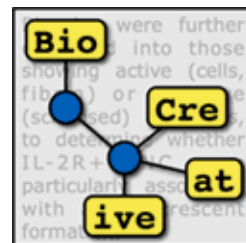
Research Associate Professor

Protein Information Resource

CBCB, University of Delaware

arighi@dbi.udel.edu

<http://www.biocreative.org>



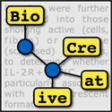
- ✚ Overview of BioCreative Effort
- ✚ Evolution of Tasks
- ✚ Impact of BioCreative
- ✚ BioCreative User Interactive Task
- ✚ Concluding Remarks



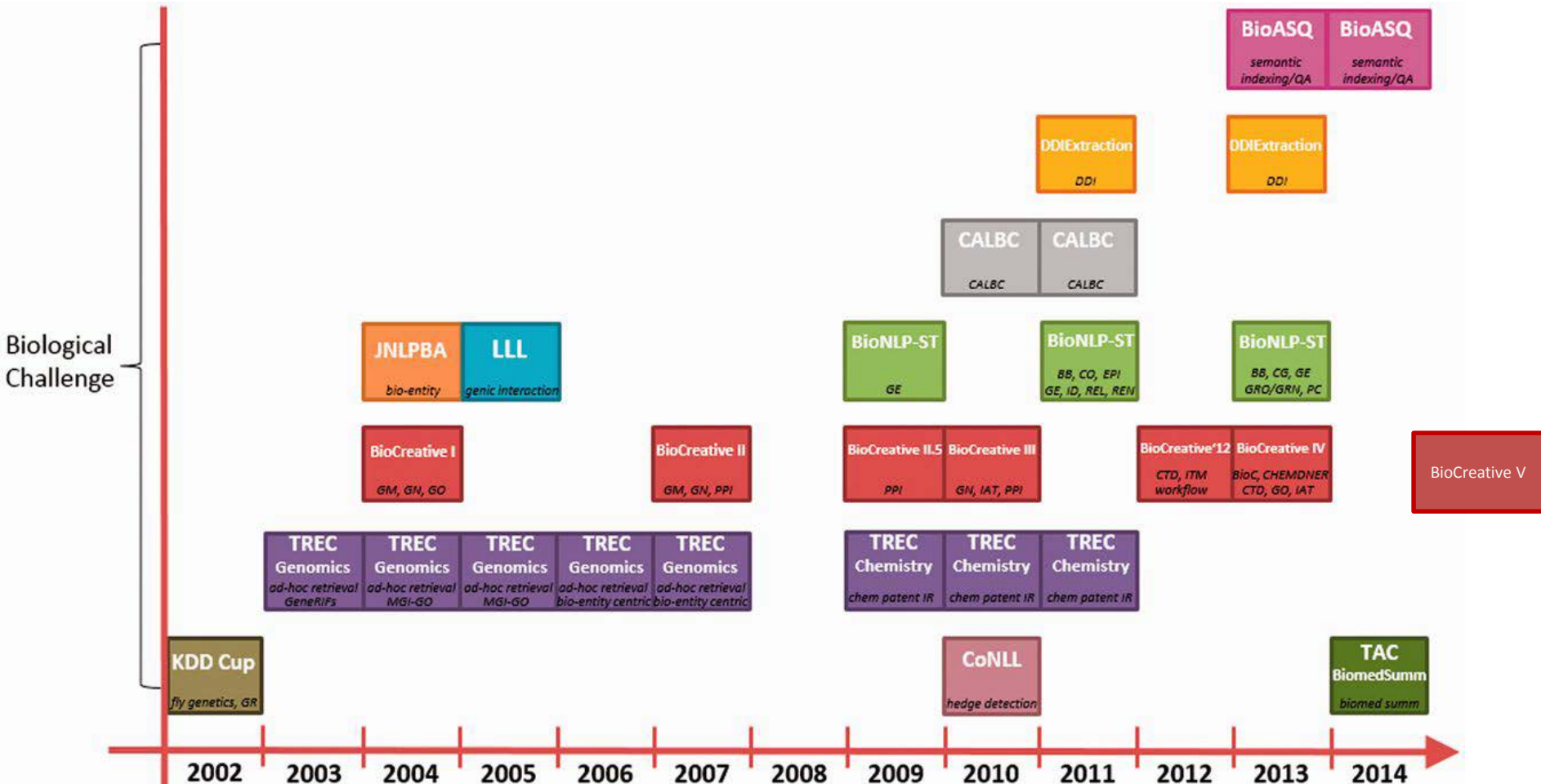
BioCreative

Community-wide effort for evaluating text mining systems applied to the biomedical domain
Collaborative and interdisciplinary effort

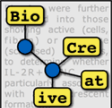




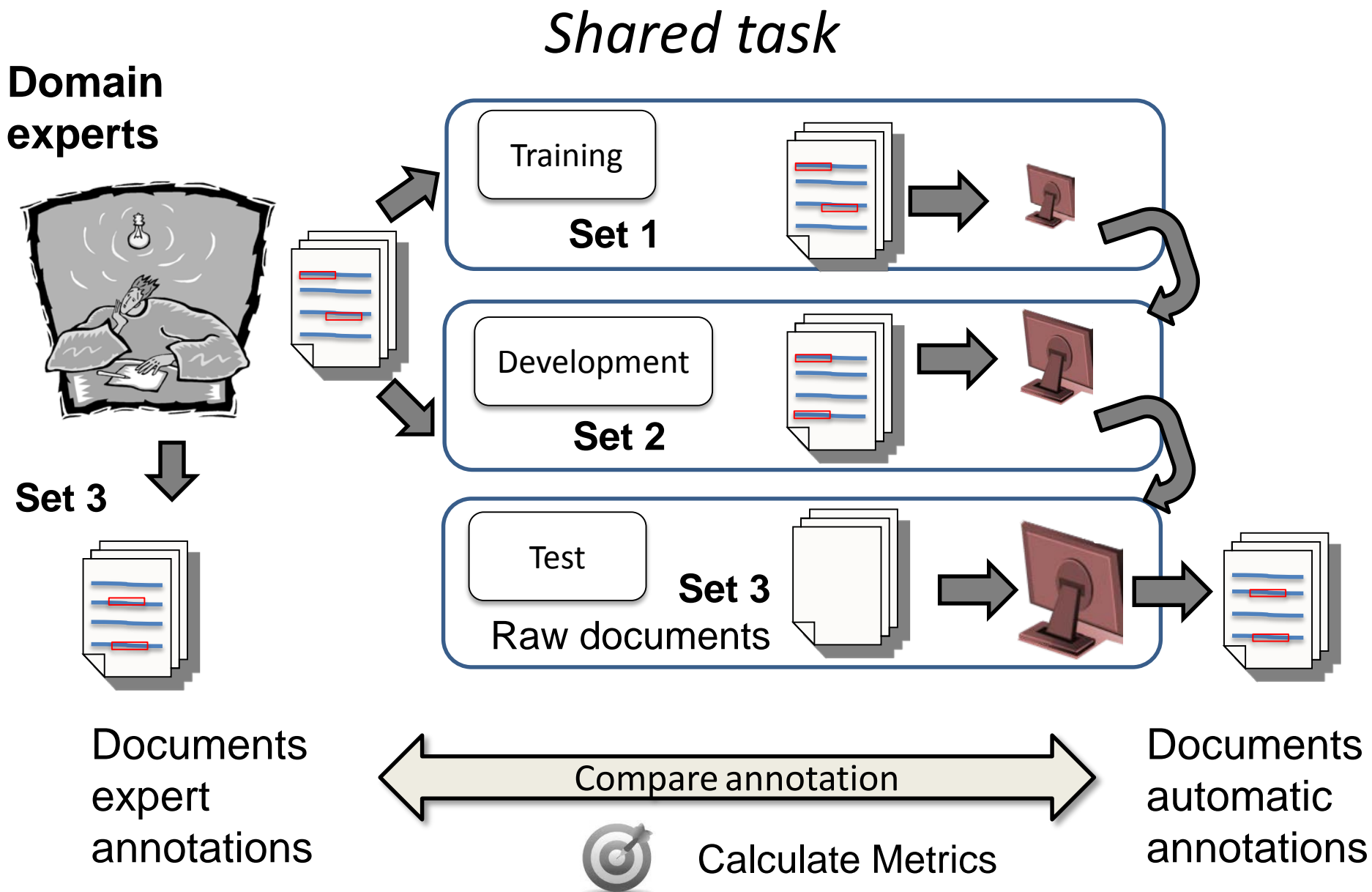
BioNLP challenges in chronological order



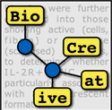
Adapted from Chung-Chi Huang, and Zhiyong Lu Brief Bioinform 2015; bib.bbv024



Traditional Tracks in BioNLP Challenges



What is special about BioCreative?



Intends to:

- Attract researchers from both natural language processing and biomedical domain
- Address problems of importance to the biology and bioinformatics community (focus on biocuration)
- Create legacy training and test data suites that could be used for development and benchmarking of future applications
- Allow the assessment of the state-of-the-art on real biological tasks

• Design of tracks based on user needs

GO curation: identification of articles with curatable GO information

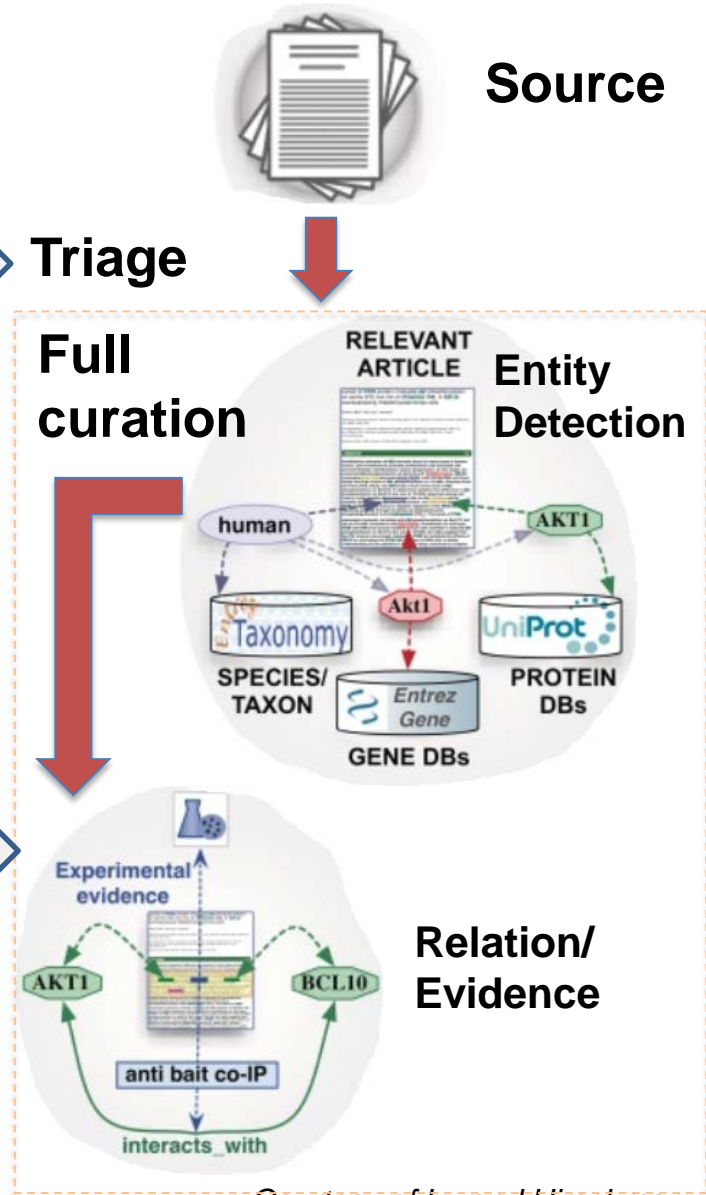
PPI curation: selection of relevant PPI articles from PubMed

CTD: identification of gene, chemical, disease and link to CTD vocabulary

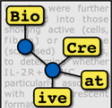
PPI curation: Extracting interactant pair, PPI method

ChemDNER: Identification of chemical entities

Generic biocuration workflow

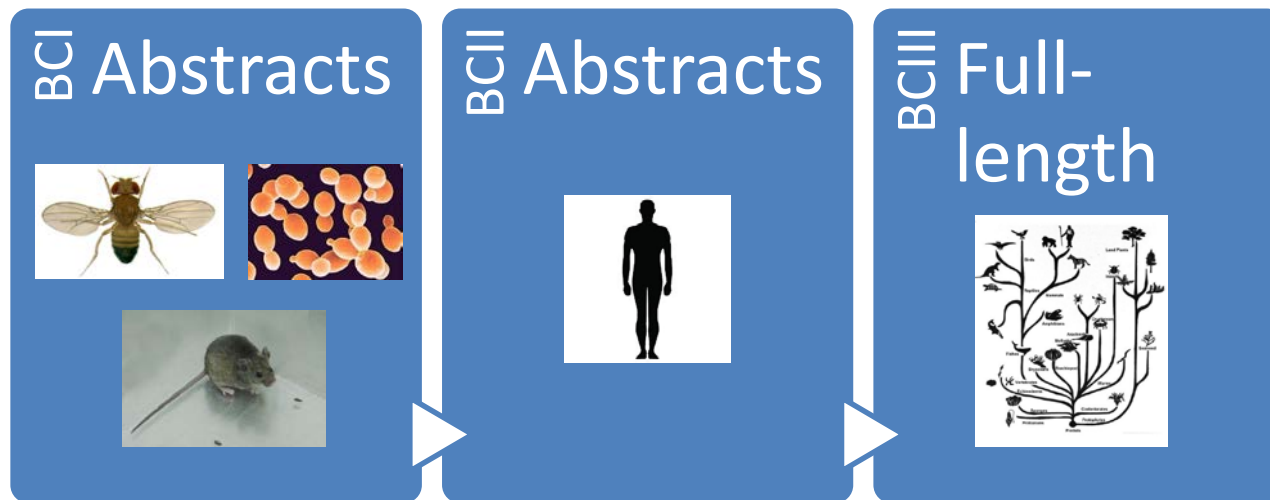


Courtesy of Lu and Hirschman



- Builds on previous tracks

Gene normalization (linking a gene mention to database identifier)

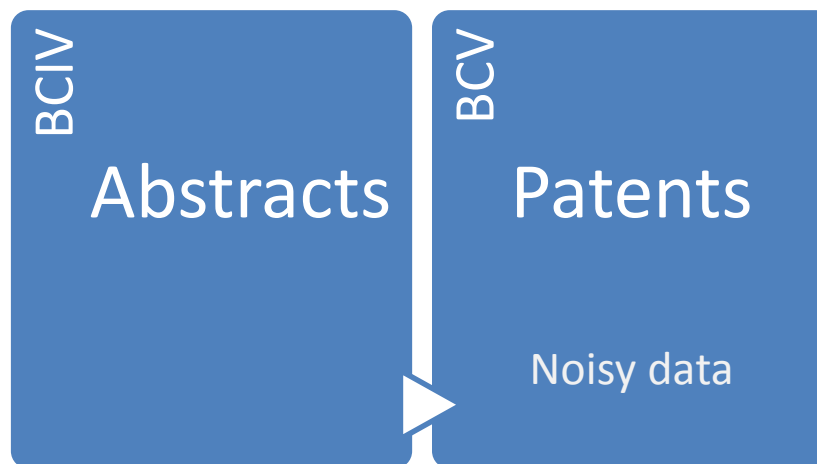


Species are known

Closer to real scenario

Chemical recognition

(identifying compound names in text)





- **Fosters interoperability**

Some problems faced by shared-task challenges:

- Many different formats
- Many new projects start over
- An atmosphere of competition

The Needs?

- Common format
- Simple-to-learn software to access the format
- Sufficient resources to motivate users

A Solution

- A convenient format to share text documents and annotations
- A library to promote interoperability of data and tools



- DTD example

PMID: 22187158

Tat mostly activated the MIP-1alpha expression in a p65-dependent manner.

Gene Name

```
<annotation id = "G0">
  <infony key="type">Gene_name</infony>
  <location offset="0" length="3" />
  <text> Tat</text>
</annotation>

<annotation id = "G1">
  <infony key="type">Gene_name</infony>
  <location offset="25" length="10" />
  <text> MIP-1alpha</text>
</annotation>

<annotation id = "G2">
  <infony key="type">Gene_name</infony>
  <location offset="52" length="3" />
  <text> p65</text>
</annotation>
```

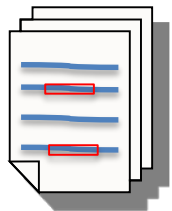


- Explores text mining systems via users

BioNLP evaluations have focused on isolated tasks, they have emphasized 'off-line' accuracy measures

But in the biocuration world....

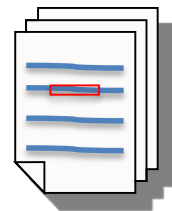
Documents automatically annotated, or retrieved by TM



Reviewed by curator



Curated document



Information stored in DB



Interactive Task (IAT): Evaluation of text mining systems by potential users and report on performance and usability

BioCreative goes beyond the shared task

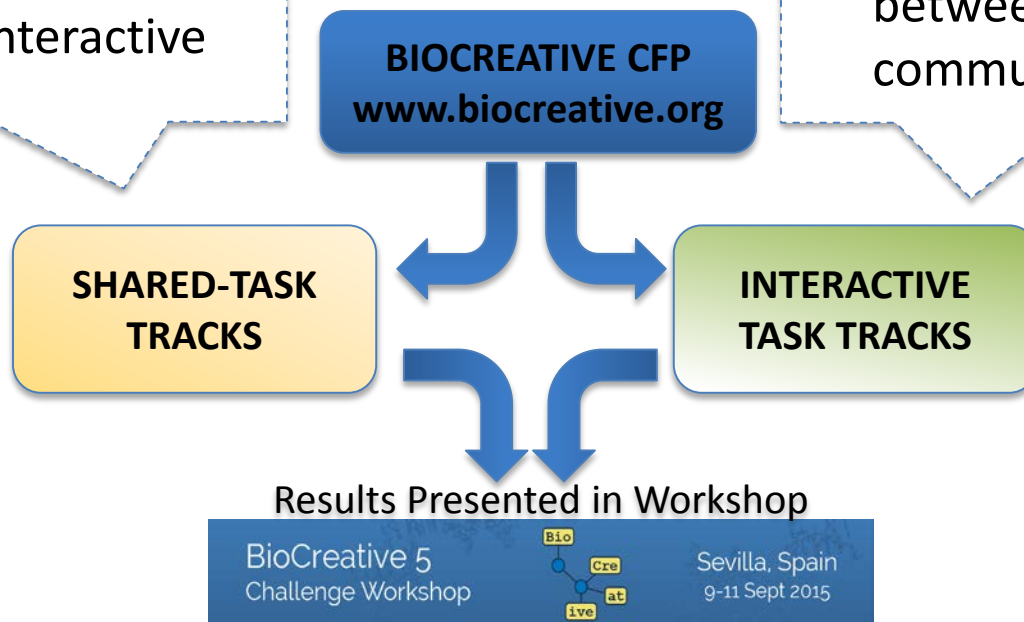


Competitive

- Task relevant to biomedical domain
- Drive state-of-the-art TM tools development
- Provide building modules for systems in interactive task

Non-competitive

- System development for literature curation tasks
- Tested by users
- Foster interaction between bioNLP and user communities



		Tasks	Publications
BC I	Spain, 2004	<ul style="list-style-type: none"> • Gene Mention • Gene Normalization • GO 	BMC Bioinformatics 2005, 6 (Suppl 1)
BC II	Spain, 2007	<ul style="list-style-type: none"> • Gene Mention • Gene Normalization • Protein-protein Interaction 	Genome Biology 2008, 9 (Suppl 2)
BC II.5	Spain, 2009	Protein-Protein Interaction: <ul style="list-style-type: none"> • Interactor Normalization • Interaction Pair • Article Categorization 	IEEE Transactions in Computational Biology and Bioinformatics 2010
BC III	USA, 2010	<ul style="list-style-type: none"> • Gene Normalization • User Interactive Task • Protein-protein Interaction 	BMC Bioinformatics 2011
BC 2012	USA, 2012	<ul style="list-style-type: none"> • CTD • Biocuration Workflow • User Interactive Task 	Database Virtual Issue 2012
BC IV	USA, 2013	<ul style="list-style-type: none"> • Interoperability • ChemDNER • CTD • GO • User Interactive Task 	Database Virtual Issue 2014 Chemical Informatics

BioCreative V Challenge Workshop

<http://www.biocreative.org/>

Bio were further into those showing active (cells, rib.) or (killed) to cell. 1L-2R+ particular assessment with formal

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[Login](#) | [Register](#)

Critical Assessment of Information Extraction in Biology - data sets are available from [Resources/Corpora](#) and require [registration](#).

[News](#) [About](#) [Events](#) [Tasks](#) [Resources](#) [Team](#)

BioCreative V

BioCreative V Workshop (Events) [2015-06-01]

The BioCreative V Workshop [website](#) is now open for [registration](#). Please visit the website for details about the [submission process](#), the [venue](#), and other information. The workshop program will be announced soon.

BioCreative 5 Challenge Workshop

Sevilla, Spain
9-11 Sept 2015

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E-mail Password [Login](#)

Welcome

Critical Assessment of Information Extraction in Biology (BioCreative) is a community-wide effort for evaluating text mining and information extraction systems applied to the biological domain.

Come to Seville

General Information
Venue
About Seville
How to get to Seville
Past Workshops
Registration
Submissions

By Topic

- News
- Events
- Resources
- Team

By Chapter

- BC Workshop '12
- BCBioCuration2014
- BioCreative I
- BioCreative I
- BioCreative II
- BioCreative II.5

Track 1- Collaborative BioCurator Assistant Task (BioC)

Goal:

Build a complete system to assist BioGrid curation

Subtasks:

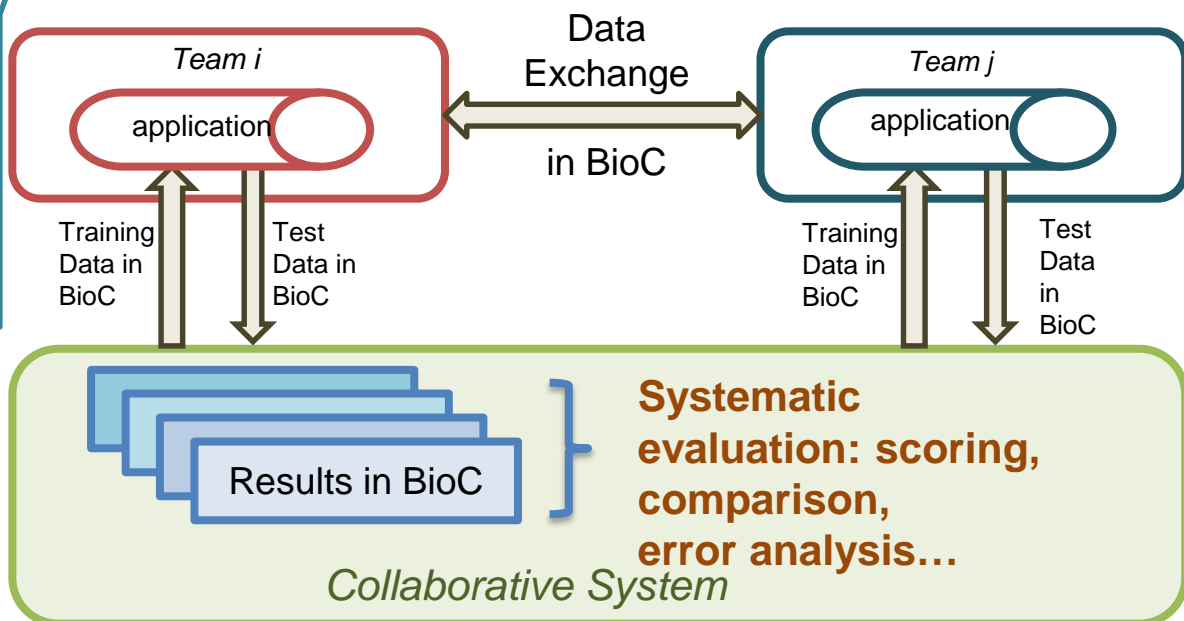
- Protein, organism
- Physical, genetic interaction
- Experimental method
- Visualization tool

Corpora:

- PubMed abstracts
- PubMed Central full text articles

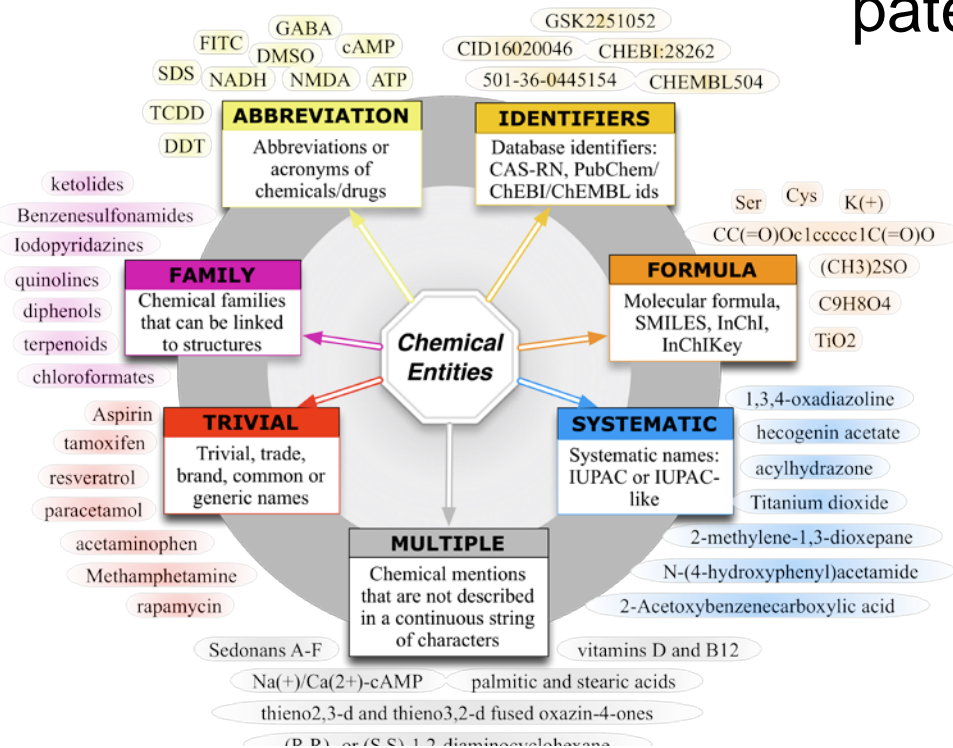
Task Organizers:

Sun Kim, Rezarta Islamaj Doğan, Donald C. Comeau, W. John Wilbur (NCBI), Andrew Chatr-aryamontri (BioGrid)



Track 2- CHEMDNER Patents

Goal: Automatic extraction of chemical and biological data from patents



Task Organizers:

Martin Krallinger & Alfonso Valencia (CNIO), Florian Leitner (UPM), Obdulia Rabal & Julen Oyarzabal (CIMA)

Builds on successful task on abstracts 3,000 abstracts test set, 91% inter-annotator agreement. F-score 87.39%

Corpora: 30,000 manually annotated medicinal chemistry patent abstracts

Subtasks:

- **CEMP subtask** (chemical entity mention in patents)
- **CPD subtask** (chemical passage detection): the detection patent abstracts mentioning chemicals (text classification/triage)
- **GPRO subtask** (gene and protein related object task): gene/protein mentions

Track 3- Chemical-disease relation (CDR)

Goal: Advance the field in relation extraction from biomedical literature

Task Organizers:

Zhiyong Lu (NCBI),
Thomas Wieggers (CTD)

Subtasks:

- Disease Named Entity Recognition
- Chemical-induced disease relation extraction

PubTator

PMID:1420741
Publication: Alimentary pharmacology _ therapeutics; 1992 Aug ; 6(4) 495-502

[Disease MESH](#)
[Chemicals](#)

Curatable
 Not Curatable
 TBD

Disease Chemical

TITLE:
Treatment of Crohn's disease with fusidic acid: an antibiotic with immunosuppressive properties similar to cyclosporin.

ABSTRACT:
Fusidic acid is an antibiotic with T-cell specific immunosuppressive effects similar to those of cyclosporin. Because of the need for the development of new treatments for Crohn's disease, a pilot study was undertaken to estimate the pharmacodynamics and tolerability of fusidic acid treatment in chronic active, therapy-resistant patients. Eight Crohn's disease patients were included. Fusidic acid was administered orally in a dose of 500 mg t.d.s. and the treatment was planned to last 8 weeks. The disease activity was primarily measured by a modified individual grading score. Five of 8 patients (63%) improved during fusidic acid treatment: 3 at two weeks and 2 after four weeks. There were no serious clinical side effects, but dose reduction was required in two patients because of nausea. Biochemically, an increase in alkaline phosphatases was noted in 5 of 8 cases (63%), and the greatest increases were seen in those who had elevated levels prior to treatment. All reversed to pre-treatment levels after cessation of treatment. The results of this pilot study suggest that fusidic acid may be of benefit in selected chronic active Crohn's disease patients in whom conventional treatment is ineffective. Because there seems to exist a scientific rationale for the use of fusidic acid at the cytokine level in inflammatory bowel disease, we suggest that the role of this treatment should be further investigated.

[CTD relation GOLD](#)

Chemical	Disease	TM	Keep	Remove	Update
Fusidic Acid (D005672)	Nausea (MESH:D009325)	M	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>

Concept View Mention View [Add bio-relation annotation to the table below.](#)

Entity type	Entity mention	Concept ID	Nomenclature	CMD	Delete	Evidence	Comment
Disease	Crohn's disease	D003424	MEDIC (Mention)	<input type="checkbox"/>	Delete	Evidence	
Chemical	cyclosporin	D016572	MESH (Mention)	<input type="checkbox"/>	Delete	Evidence	
Chemical	Fusidic acid fusidic acid	D005672	MESH (Mention)	<input type="checkbox"/>	Delete	Evidence	
Disease	inflammatory bowel disease	D015212	MEDIC (Mention)	<input type="checkbox"/>	Delete	Evidence	
Disease	nausea	D009325	MEDIC (Mention)	<input type="checkbox"/>	Delete	Evidence	

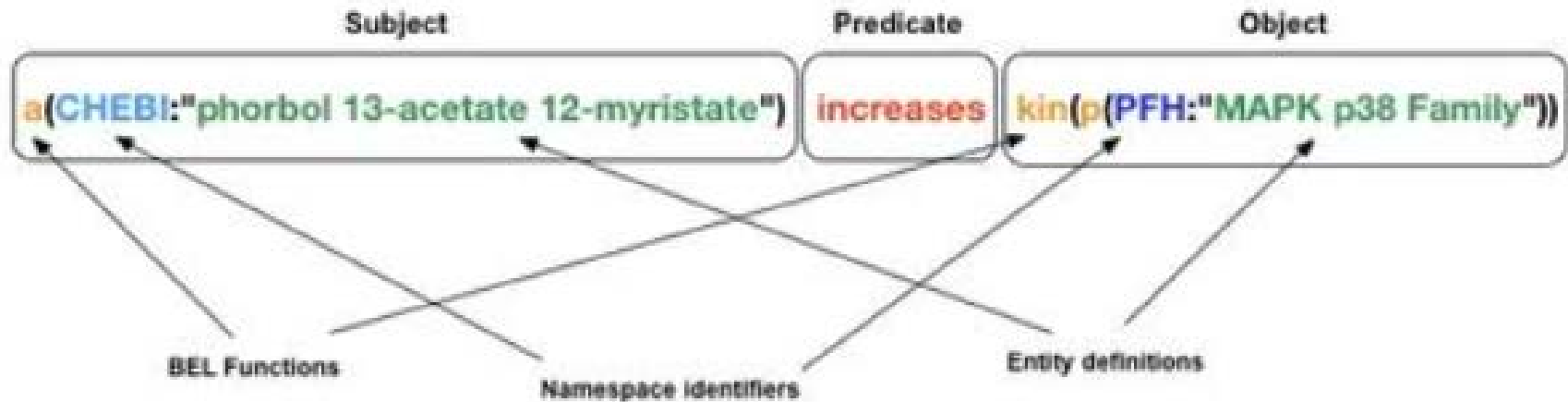
Track 4- Causal Networks in BEL

What is BEL?

Biological Expression Language
Computable knowledge representation

Task Organizers:

Fabio Rinaldi (UZurich)
Juliane Fluck (Fraunhofer)



Corpus: 50 biological networks, 180,000 relationships

Subtasks:

- Generation of BEL statements given the evidence
- Find evidence for a given BEL statement

Track 5- User Interactive Task

Task Organizers:

Cecilia Arighi, Qinghua Wang (PIR, UDel) and Lynette Hirschman (MITRE)

Evaluation of text mining tools by users

It is a *demonstration interactive* task

Need to involve users



User Advisory Group (UAG)

A diverse sample of end users with multiple text mining needs

- Help to develop end user requirements for interactive text mining tools
- Serve as users for the interactive task
- Assist in corpora annotation for biocreative tasks
- Help in recruiting biocurators

UAG BioCreative V

Chairs: Cecilia Arighi and Zhiyong Lu

Andrew Chatr-aryamontri

Raul Rodriguez-Esteban

Stan Laulederkind

Sherri Matis-Mitchell

Johanna McEntyre

Peter McQuilton

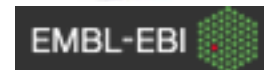
Evangelos Pafilis

Sandra Orchard

Sangya Pundir

Mary Schaeffer

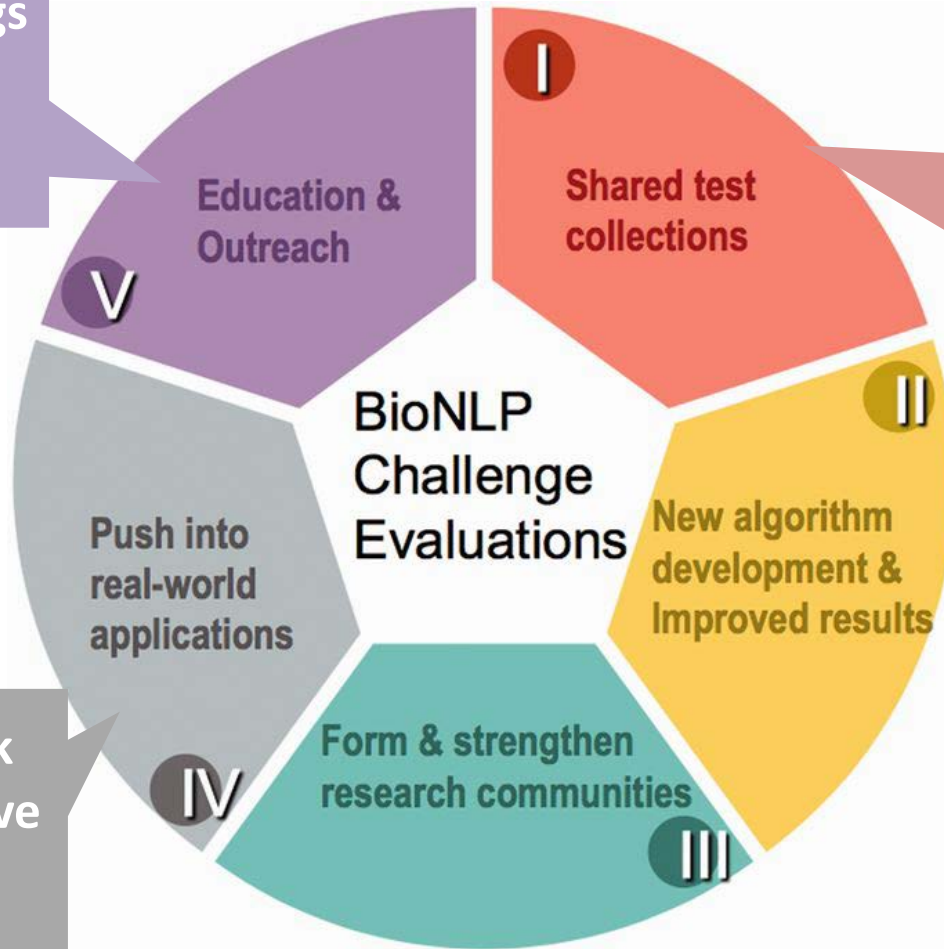
Kimberly Van Auken





Impact/contributions

Workshops at scientific meetings
Webinars (BioC)
Publications



BioC corpora
GN corpora
PPI corpora
CTD/CDR corpora
ChEMDNER corpora

Interactive Task
BioC collaborative task

Modified from Chung-Chi Huang, and Zhiyong Lu Brief Bioinform 2015;bib.bbv024

Published by Oxford University Press 2015. This work is written by US Government employees and is in the public domain in the US.



II- New Developments

BioCreative has promoted the development for state-of-the-art solutions

- Gene Mention: AIIA-GMT
- Gene Normalization: GNAT, GenNorm, ProMiner
- PPI triage: PIE
- GO categorization: GoCat

A variety of methods have been applied:

- Markov models
- Machine learning
- Rule-based
- Naïve Bayes classifiers
- Support Vector Machine



II- Experiment with New Metrics

Threshold Average Precision (TAP-k)

In Gene normalization BioCreative III

Derivative of Mean average precision (MAP) with a threshold determined by the first k errors in the ranked list.

TAP- k is able to measure ranking, reflect the user tolerance of prediction errors (false positives), as well as make use of confidence scores.

Hierarchical Precision, Recall and F scores

In Gene Ontology task BioCreative IV

Given the hierarchical nature of GO, considers common parent terms in computer-predicted and human-annotated GO terms



IV-Form and strengthen research communities

Successful BioNLP-user interactions through BioCreative

PubTator

Used by NLM for indexing. Currently being used by UniProt curators

TagTog

Gene indexing in Flybase (Cejuela et al., PMID:24715220)

ODIN

In PharmGKB workflow (Rinaldi et al., PMID: 22529178) now being tested on RegulonDB for BioCreative V

RLIMS-P

Phosphogrid curation (Torii et al., PMID:25122463)



Impact/contributions

	# articles in ePMC
BioCreative Editorials	6
BioCreative mentioned in title or abstract	148
BioCreative is found in reference section	389

Top 10 MeSH terms in articles referencing BioCreative	Frequency
Humans	119
Natural Language Processing	98
Algorithms	81
Databases (Factual, genetic, protein)	79
Software	78
Computational Biology/methods	69
Vocabulary, Controlled	61
Artificial Intelligence	60
Information Storage and Retrieval/methods	51
Data Mining/methods	50



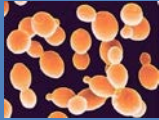



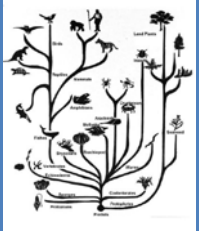
Gene Normalization in BioCreative

Convention for protein naming are different in different organisms. Differ in number of synonyms, in complexity of names,

BC I

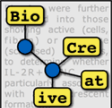
BC II

BC III

					
F-Score	0.92	0.82	0.79	0.81	0.50
IAA %	87	91	69	91	-
Average synonyms per identifier	1.86	2.94	2.48	5.5	
Average synonym length in words	1	1.47	2.77	2.17	

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2559987/>

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3269937/>



GO task

Overall statistics of the annotated corpus grouped by data sets

Data set	Articles	Genes (unique)	GO terms (unique)	Evidence text passages w.r.t. GO Gene Unique
Training set	100	316	611	2440 2478 1858
Development set	50	171	367	1302 1238 964
Test set	50	194	378	1763 1677 1253
Total	200	681	1356	5505 5393 4075

Genes	GO terms	Exact match			Hierarchical match		
		P	R	F ₁	hP	hR	hF ₁
172	860	0.117	0.157	0.134	0.322	0.356	0.338
172	1720	0.092	0.245	0.134	0.247	0.513	0.334
172	3440	0.057	0.306	0.096	0.178	0.647	0.280
50	2639	0.018	0.075	0.029	0.064	0.190	0.096
46	1747	0.024	0.065	0.035	0.087	0.158	0.112
23	37	0.108	0.006	0.012	0.415	0.020	0.039

IAA GO term selection
47% strict
62% hierarchical

Yuqing Mao et al. Database 2014; bau086

Van Auken et al., Database 2014, bau074



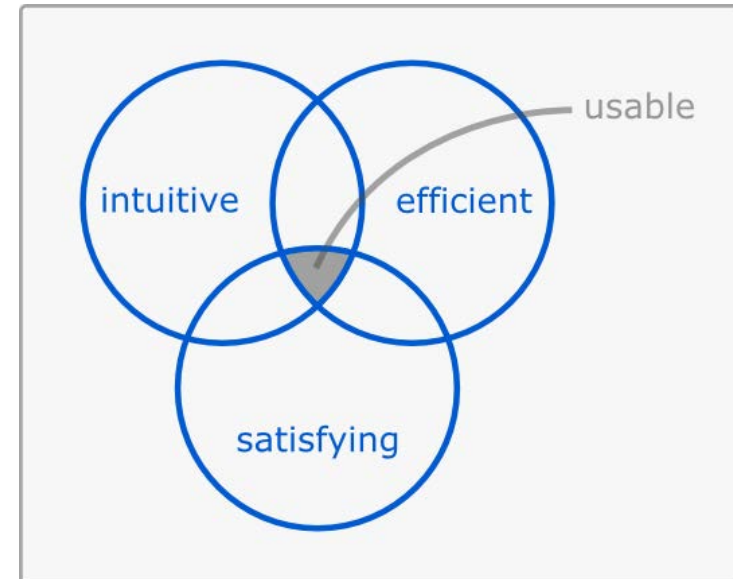
General Remarks

- The Tasks have evolved to resemble more the real scenario
- Improvements have been achieved in many tasks
- Combination of methods usually improves the performance
- Although results are not of sufficient quality to use as an entirely automated process, output from these tools can provide a head start for curators

Can text mining tools help in Biocuration



Our idea is to expose text mining systems to biocurators so they can provide feedback on the system and become adopters in the future



Two levels of user participation

Partial

Follow pre-defined tasks aimed at testing system usability

Complete user survey

Collate outputs

Full

Training via demo, examples, help document, annotation guidelines, and output format

Practice with examples, report bugs

No

Yes

Is biocurator familiar with system and annotation ?

Dataset selected by domain expert (or coordinator)

1/2

1/2

Non TM-assisted Annotation

TM-assisted Annotation

Complete user survey

Collect outputs and calculate metrics



User Survey

Based on Questionnaire for User Interface Satisfaction (QUIS)

Five main categories:

1. Overall reaction
2. System's ability to help complete tasks
3. Design of application
4. Learning to use the application
5. Usability

Goal: Try to find correlation of response to questions in survey with overall system satisfaction to learn what aspects are important to users

<http://ir.cis.udel.edu/biocreative/survey.html>

<http://ir.cis.udel.edu/biocreative/survey2.html>



Highlights of Previous Runs

1-Match between system and the real world (of Biocuration)

- The system should speak the users' language rather than system-oriented terms
- Systems should follow standards of its user community
- Sentence vs. Document level annotation

2-Testing the Systems NOT the Users

- Participants not being tested. But in the context of this activity we need to distinguish the participants into curation novice vs. expert because it has an impact on the performance

3-Documentation: Annotation guidelines and tutorials

- Provide detail annotation guidelines for the task
- Provide tutorial for system training with hands-on examples



Highlight of Previous Runs

4-System performance and functionalities in interface

- System performance is a key aspect to biocurators, but coupling results with functionalities that assist in easily correcting or finding additional information is very important for an interactive system

5-System Output

- To be useful for curation annotated results should be exported in standard formats that can be further utilized in the curation workflow. Tab-delimited and BioC formats were requested.

Metrics:

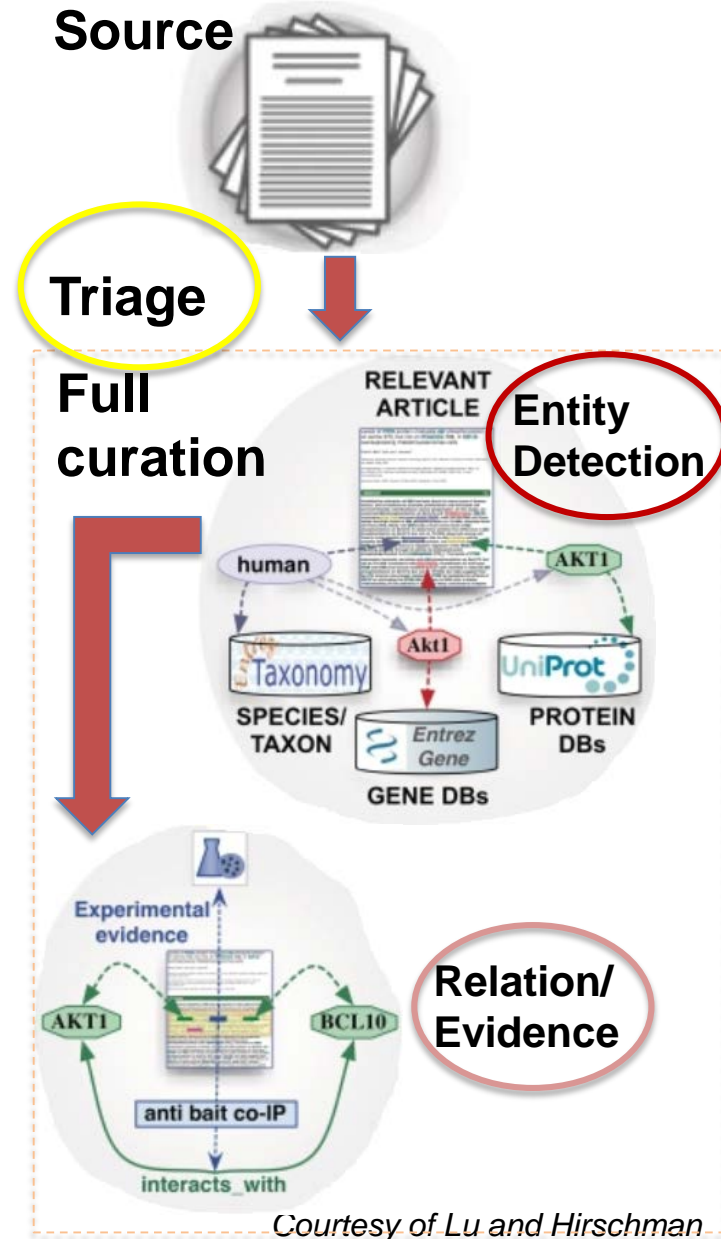
Time on task (objective)

Preference via survey (subjective)

Participating Systems in BioCreative IV



System	Description of the tool
	Cell Finder Annotation of gene, expression relation and cell type in text snippets from a set of articles
	Ontogene Detection of Gene/Chemical/Diseases and their interactions
	MarkerRIF Retrieval of articles about biomarkers, and extraction of disease and biomarker (gene) with normalization
	SciKnowMine Triage based on pre-trained categories of interest in full length articles
	BioQRator Retrieval based on relevance on protein-protein interaction information and annotation of protein pair
	RLIMS-P Triage on protein phosphorylation. Annotation of kinase, substrate and site with normalization.
	Egas Identification and extraction of protein-protein interaction events described over PubMed abstracts related to neuropathological disorders
	tagtog Annotation of gene names within full-text documents especially machine-predicted documents
	Argo Annotation of metabolic process-related named entities, namely chemical entities and genes or gene products



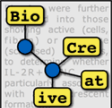
Recruitment of Biocurators

Call for participation via International Society for Biocuration (ISB) mailing list, and the ISB meeting and BioCreative websites
Personal invitation



What's in it for Biocurators?

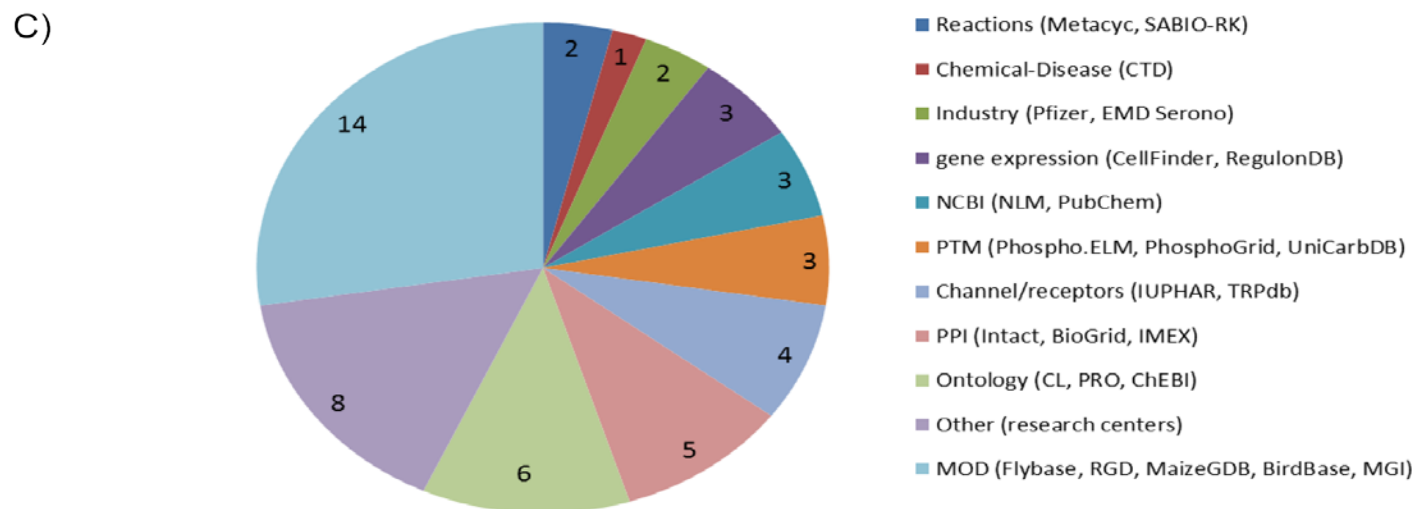
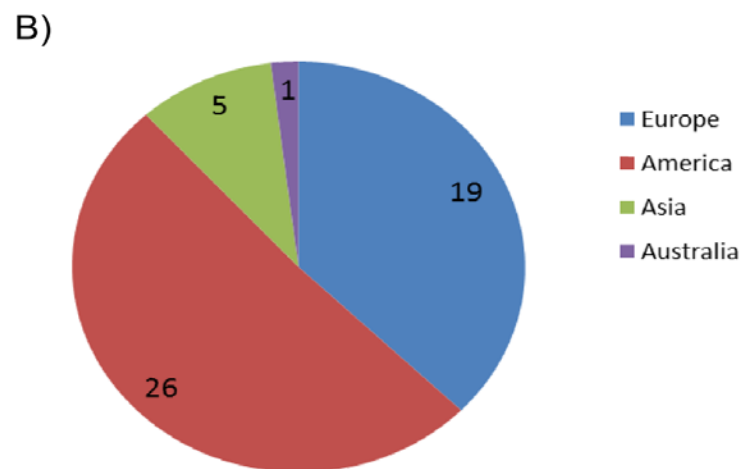
- Exposure to state-of-the-art text mining systems
- Direct communication and interaction with developers
- Contribution to tools that meet the needs of biocurators
- Adoption of text mining tool
- Potential publication in peer reviewed journal
- Focus on a set of articles that will add to their curation effort



Recruitment in BioCreative IV

A)

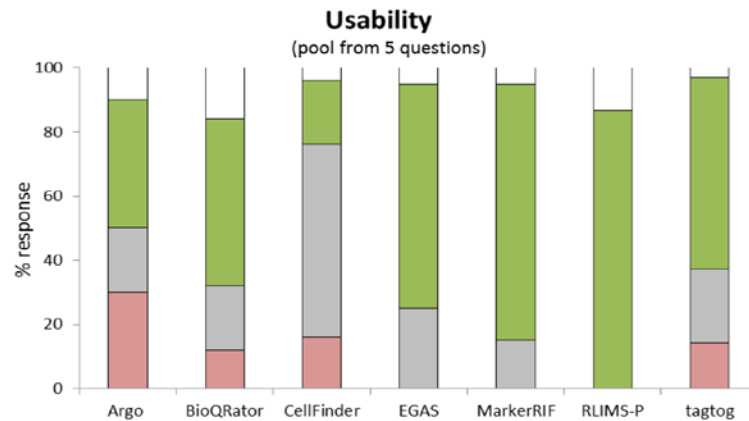
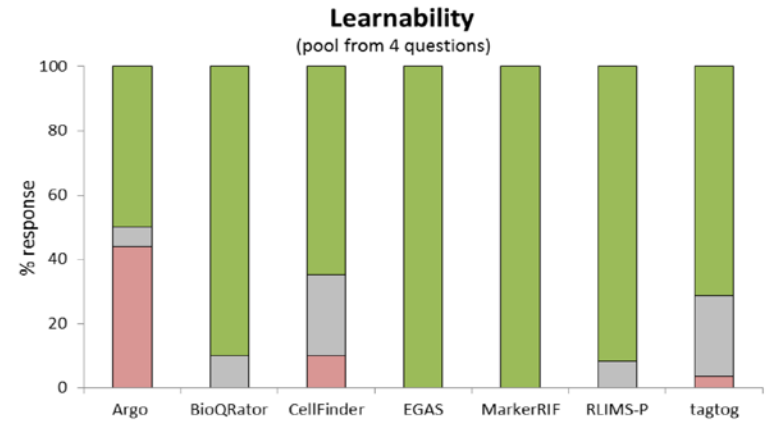
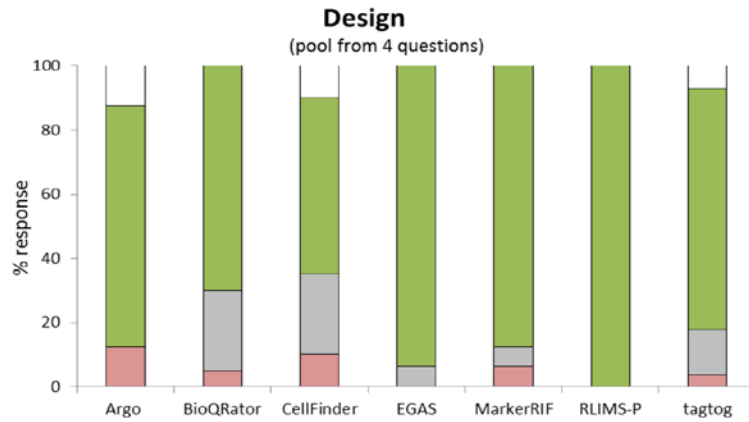
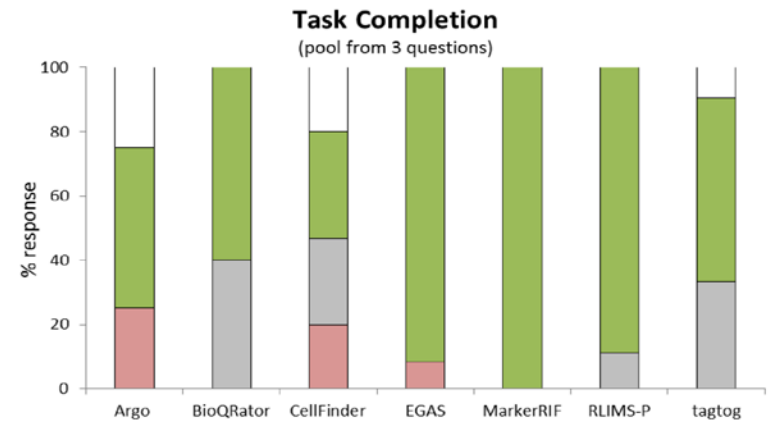
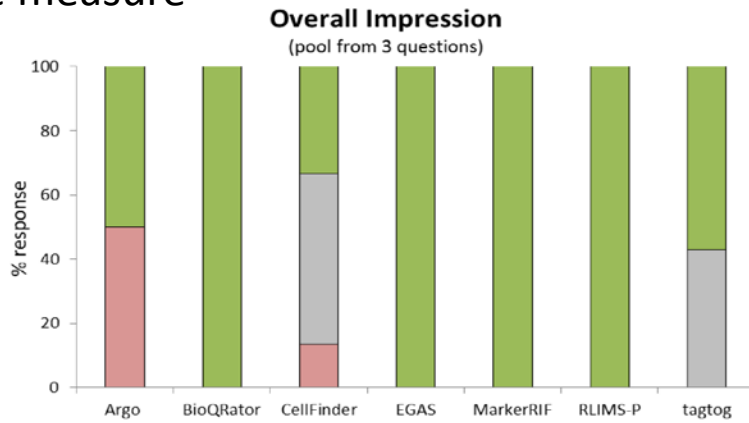
System	# Curators	
	Full	Partial
CellFinder	4	2
Ontogene	2	3
MarkerRIF	3	3
SciKnowMine	1	5
BioQRator	6	6
RLIMS-P	3	5
EGAS	4	4
Tagtog	7	2
Argo	3	1
Total	33	31



Time on task in full level participation curation task and curator experience level

System	no TM (min)	TM (min)	TM (min)	$t_{\text{noTM}}/$ t_{TM}	$t_{\text{noTM}}/$ t_{TM}	Curation experience (years)
BioQRator	275	195		1.4		<1
	70	100		0.7		>3
	160	180		0.9		>3
	150	150		1.0		1-3
Egas	93.71	60.13		1.6		<1
	184	120		1.5		1-3
	104.91	26.21		4.0		<1
	64.48	60.86		1.1		>3
MarkerRIF	212	90	145	2.4	1.5	1-3
	115	84	70	1.4	1.6	<1
	170	95	103	1.8	1.7	<1
RLIMS-P	585	560		1.0		>3
	301	186		1.6		1-3
	164	161		1.0		<1

Subjective measure



Key

- no response
- positive response
- neutral response
- negative response



Some Observations:

The curation time does not always go hand by hand with user overall system satisfaction

With BioQRator and RLIMS-P curators are satisfied with system even the time required in the no-TM-assisted versus TM-assisted curation was comparable for each.

Some reasons:

- system provides a nice interface with functionalities that in the long run makes the monotonous curation work more enjoyable
- some systems have both retrieval and extraction steps, the curators appreciated the retrieval step because it saves a lot of time in article selection. However, the task was measured on the extraction step and most time was spent on normalization.



Areas of improvement detected via usability

- System accessibility:* due to one of the following; firewalls, system temporarily down, or inability to log in.
- Error messages:* either no error message displayed or the error message did not satisfactorily explain the problem.
- Hidden functionality:* key functionality for executing the TM task not apparent to curators.
- Language and icons:* icons and names of sections/functionalities non-intuitive or used TM jargon.
- Look and feel:* Color choice for entity highlighting was not optimal for color blinded users for some of the systems



Recruiting users for IAT now!

<http://www.biocreative.org/tasks/biocreative-v/iat-task-biocurators/>

Seven Systems for different tasks

Please select one or more systems from this list:

- Argo** (Curation of phenotypes relevant to the chronic obstructive pulmonary disease (COPD) in the PhenomeNet database)
- Egas** (Identification of clinical attributes associated with human inherited gene mutations, described in PubMed abstracts)
- OntoGene** (Curators interested in bioconcepts currently supported by OntoGene, e.g., miRNA, gene, chemical, disease)
- GenDisFinder** (Knowledge discovery of known/novel human gene-disease associations from biomedical literature)
- MetastasisWay** (Look for the biomedical concepts and relations associated with metastasis and construct the metastasis pathway)
- BELIEF** (A semi-automated curation interface which supports expert in relation extraction and encoding in the modelling language BEL (Biological Expression Language))
- EXTRACT** (List the environment type and organism name mentions identified in a given piece of text)

Evaluation Period: period June 22 to July 31

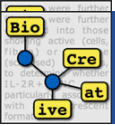
Flexible and remotely conducted

Total time commitment estimation over that period:

Full participation: 12h

Partial participation: 30min-1h

Sign In!



Concluding Remarks

Manual curation is accurate, but does not scale. Text mining scales, but is not accurate

Interactive systems like those presented in IAT can provide curators with decision support:

- suggesting important papers to curate
- highlighting entities of relevance in text
- offering controlled vocabularies and ontologies
- on-the-fly error-correction
- removal of redundancy



Concluding Remarks

- Tools developed in past BioCreative challenges have been integrated as modules in a subset of the participating systems, such as GenNorm in RLIMS-P; and PIE for protein-protein interaction article ranking and retrieval BioQRator.
- This demonstrates the importance of the traditional shared tasks to promote development of state-of-the-art text mining tasks that when mature these offer text mining solutions that can be integrated in a system framework.



BioCreative Organizers

UAG Members

Text mining teams and biocurators that participated in the BioCreative tasks

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