Bioinformatics Experimentation in a New Agent-Based Infrastructure OpenKnowledge

(poster coming soon)

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Context of the Work

OpenKnowledge (EU FP6):

A Peer-to-Peer architecture emphasizing
the sharing of knowledge via interaction models

- 3y Targeted Research Project in Computer Science
- 2006-8; currently smaller follow-on projects since
- Testbeds: Bioinformatics + Emergency Response

www.openk.org OK kernel V1.1 (requires Java 1.5; JRE6)
+ more info, examples
+ demo of “omicslab” scenario

OpenKnowledge - Bioinformatics

Robertson* / Gerloff / Tate / Bundy	University of Edinburgh
Schorlemmer / Abían / Sierra / Augusti	CSIC Barcelona
van Hermelen	Vrije Universiteit Amsterdam
Dasmahaptra / Lewis Shadbolt / Berners Lee	School of Eng & CS Southampton
Motta	Open University
Giunchiglia / Marchese / Bonifacio / Riccardi	University of Trento

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Interest in P2P

- sharing (without depositing)
- ease of joining (“subscribing”) to a task group
- scalability
- no (or less) need for curation and maintenance

P2P in bioinformatics:

- Chinook
- SEED

Other related work: Workflow Platforms

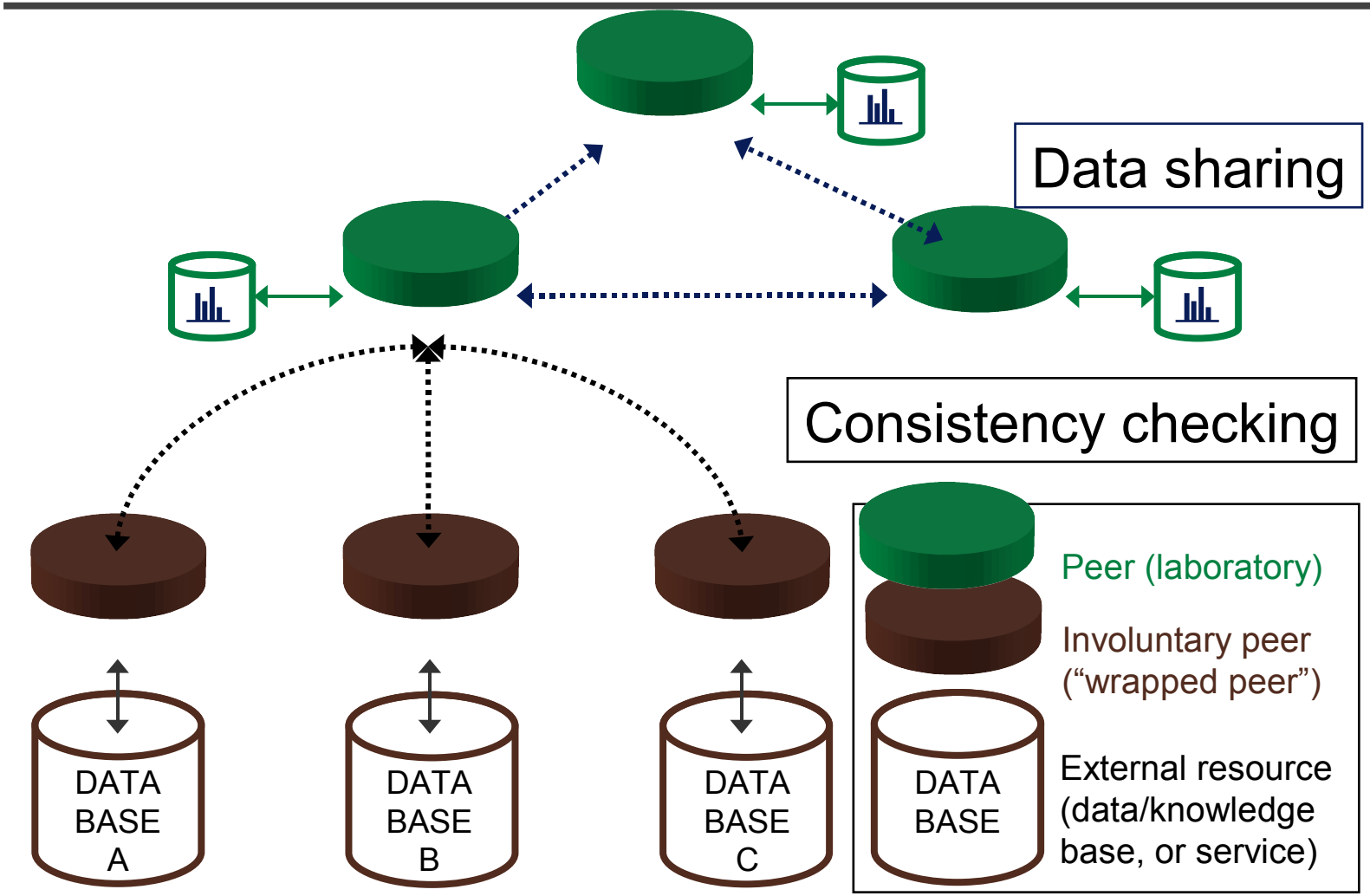
- Kepler
- TAVERNA (myExperiment)

OK - Design Philosophy & Goals

- peer-to-peer ⟺ as open as possible
- not (as) domain-oriented
- peers groups include non-expert users
  (expert / some knowledge / “dummy” users)
- emphasis on sharing knowledge/data of any kind
  (less on the distribution of computational load)

- supporting language:
  LCC (Lightweight Co-ordination Calculus):
  message passing (more details on poster)

Applied Bioinformatics/Biology at High Level: Consistency checking + Data sharing



An Interaction in OK in a Nutshell

1. Peer E (Experimenter) sets a task (asks a question)
2. Discovery Service (DS) looks for peers of potential interest, and suggests interaction partners and interaction models (IM) (if available)
3. The IM specifies roles to be played, and peers subscribe (by agreeing) to interact + in which role(s)
4. One peer is (computational) coordinator
5. Roles are executed via OK-Components (OKC)

Notes:

- many possible IMs for carrying out the same task
- OK is at "infancy" stage! For example, DS in OK currently relies on information provided by peers

Experiment A - yeast protein structure models

Extend structural knowledge through modelling:

Find fragments of 3D-models of *S.cerevisiae* (yeast) proteins that can be trusted

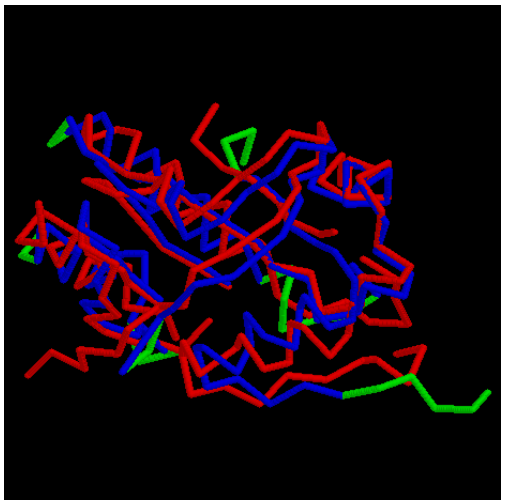
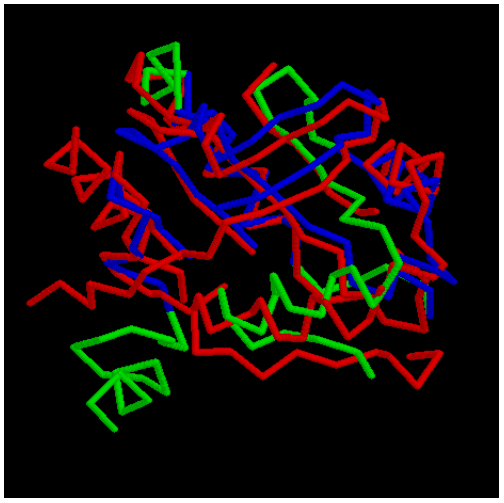
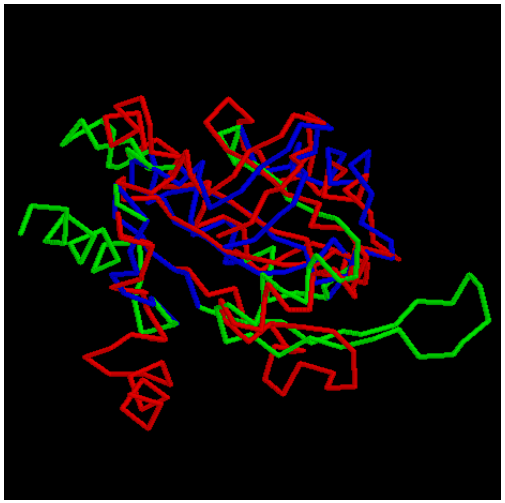
- 6604 yeast protein sequences (some predicted)
- currently only 330 known 3D-structures (in PDB)

Consensus-building is a popular strategy in Applied Structural Bioinformatics (typically via meta-WWW-servers)

- Compare modelled structures from three databases: SWISSMODEL (769 models); SAM (2211 models); ModBase (2546 models) in OpenKnowledge
- MaxSub program to identify common substructures

Results

Example: (MaxSub pair-wise common substructure in blue)

YBR024W: SWISS-SAM	ModBase-SAM	SWISS-ModBase
		
MScore: 0.660	0.459	0.400

CYSP = Comparison of Yeast 3D Structure Predictions

578 three-way supported

MaxSub-substructures > 45 aa

from 545 proteins

(Linked from www.openk.org)

Experiment C - *de novo* peptide sequencing

Look into one another's "trash"

Increase confidence in peptide assignments to MS/MS spectra in proteomics

- one (of several) uses of MS to study protein content
- especially difficult: non-model organisms; mixtures

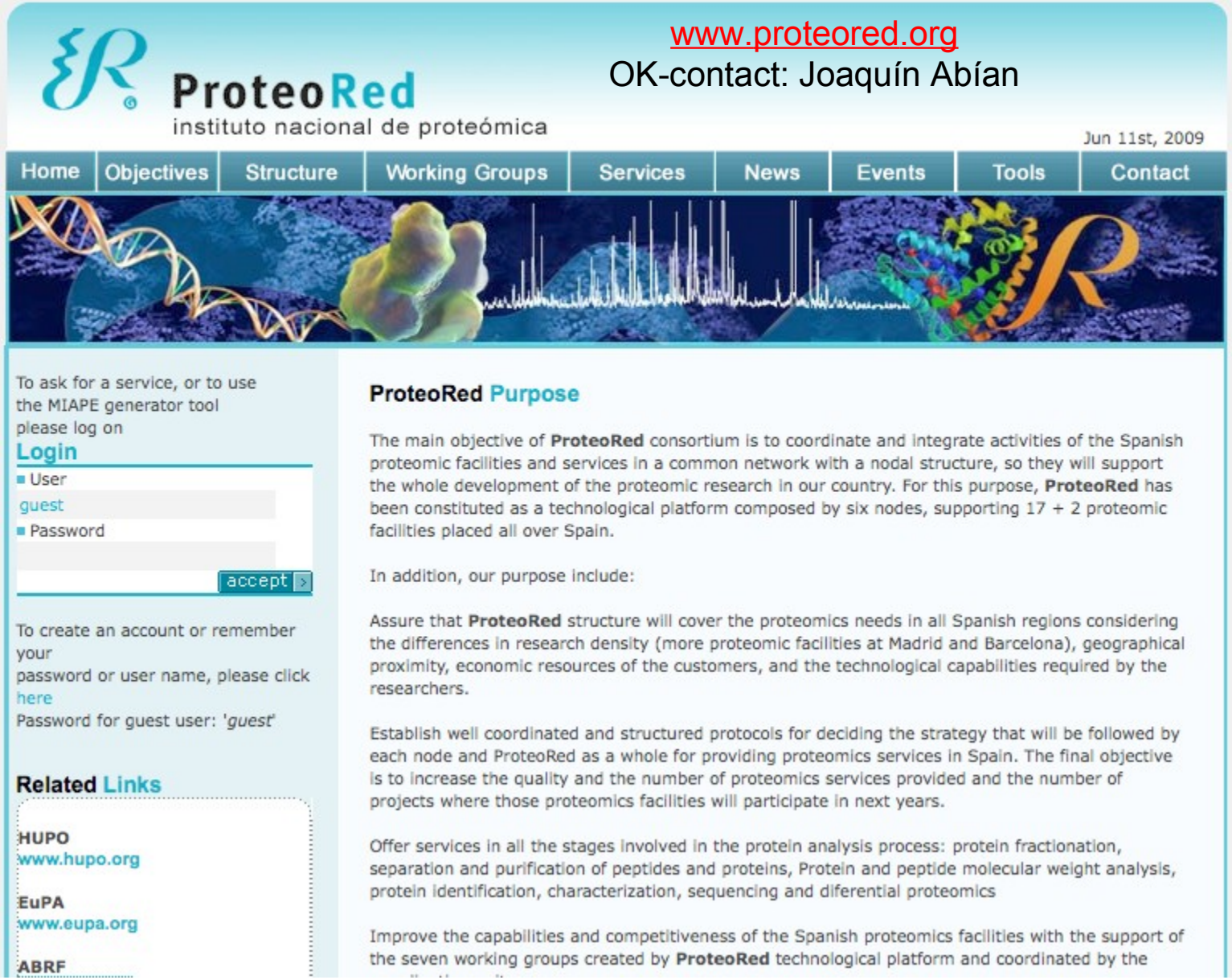
Data sharing has become a bottleneck in modern biology

- Implement demo example guided by user input
- OK-emulation with 9 peers: 7 proteomics labs + self + NCBI database
- Test data: 38 peptides from ABRF 2006 (contest data; 35% of 78 labs identified >40 or 48 proteins in 2006)

Contact/input from an active community

www.proteored.org

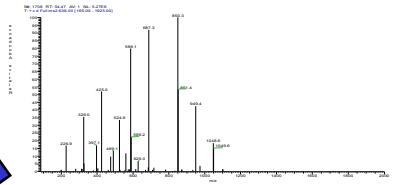
OK-contact: Joaquín Abían



Experiment C: de novo peptide sequencing

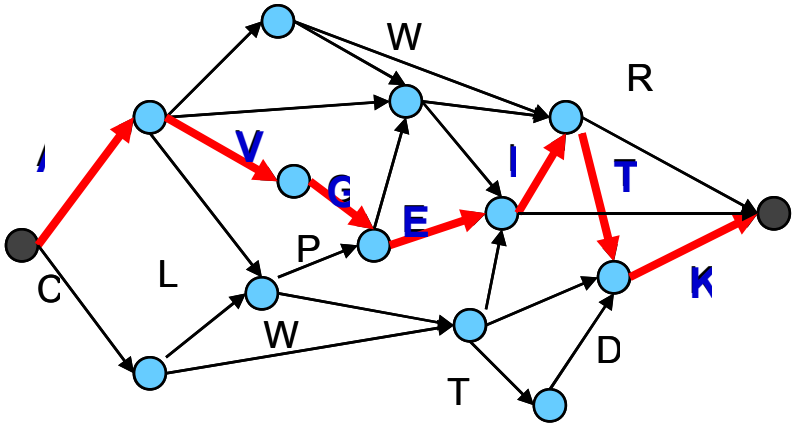
Database Search

BLAST or OMSSA



"de novo"

PepNovo, Lutefisk, PEAKS, MASCOT



Database of known peptides

MDERHILNM, KLQWVCSDL, PTYWASDL, ENQIKRSACVM, TLACHGGEM, NGALPQWRT, HLLERTKMNVV, GGPASSDA, GGLITGMQSD, MQPLMNWE, ALKIIMNVRT, **AVGELTK**, HEWAILF, GHNLWAMNAC, GVFGSVLRA, EKLNKAATYIN..

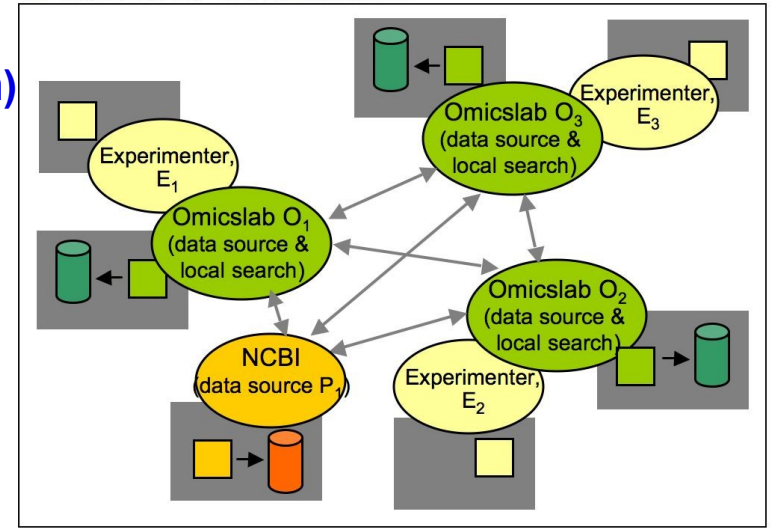
AVGELTK

Results

Implementation notes:

- **search is executed locally using BLAST (sequence) or OMSSA (spectrum)**
- **visualisation: OK-omics prospector**
- **database peer is important for revealing contaminants + holds promise for consistency checks with other data (species, annotation, etc)**

3Labs and 1Database:



Successful integration of data sharing and consistency checking

We found increased correct identification rate compared to random chance, though not yet significant

Encouragement to run a larger sample

(Demo available at www.openk.org)

Conclusions & Future Work

- Three implementation examples served primarily to:
  - as proof of principle (can be done) & demos
  - to advance OK-development
  - to illustrate complementarity to other infrastructures
  ⇨ benefit from each other's experiences
- Particularly exciting:
  - data sharing example
  - work with data other than sequences (i.e. not strings)
- UCSC group's current/future interests:
  - spur on development and user-base through more integrated examples
  - investigate benefits of raw data sharing (J.Magasin)