CARSTEN KETTNER

TOWARDS A DATABASE FOR FUNCTIONAL ENZYME DATA

STRENDA DB

E-SCIENCE DAYS 2017 – HEIDELBERG

BEILSTEIN INSTITUT

CARSTEN KETTNER

PROPOSING THE CHANGE OF A PARADIGM

STRENDA DB

E-SCIENCE DAYS 2017 – HEIDELBERG

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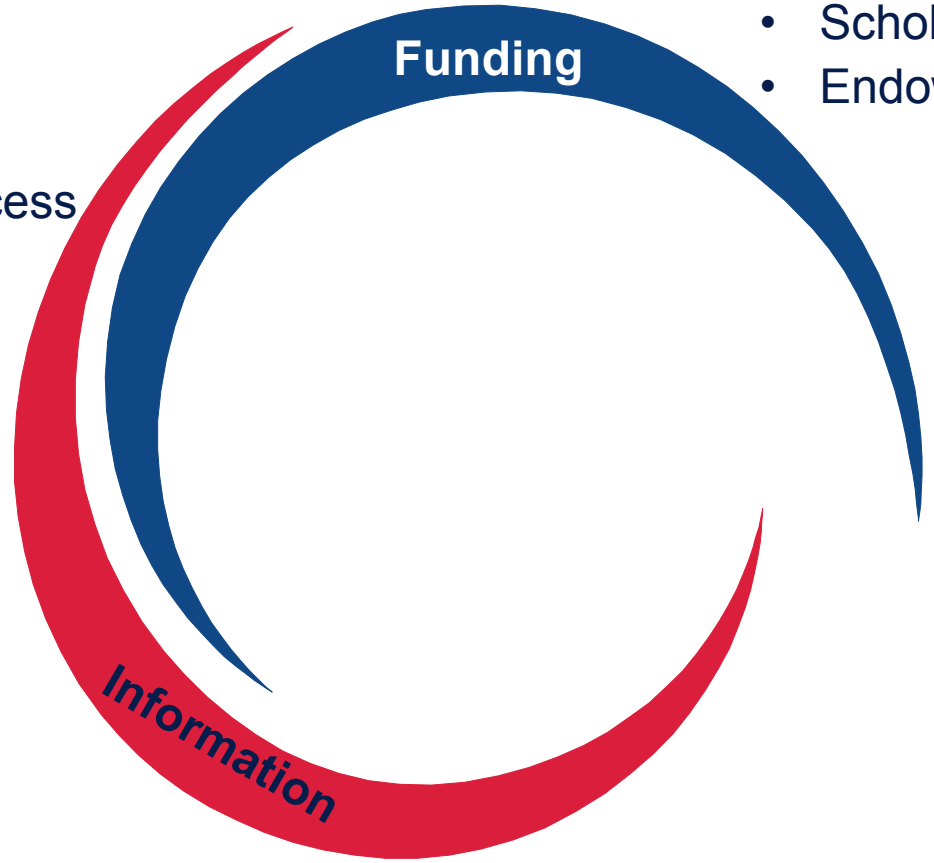
Beilstein-Institut

- Platinum Open Access Journals
- Beilstein TV
- STRENDA
- MIRAGE

Beilstein-Institut

- Projects
- Scholarships
- Endowed Professorships



- Platinum Open Access Journals
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- STRENDA
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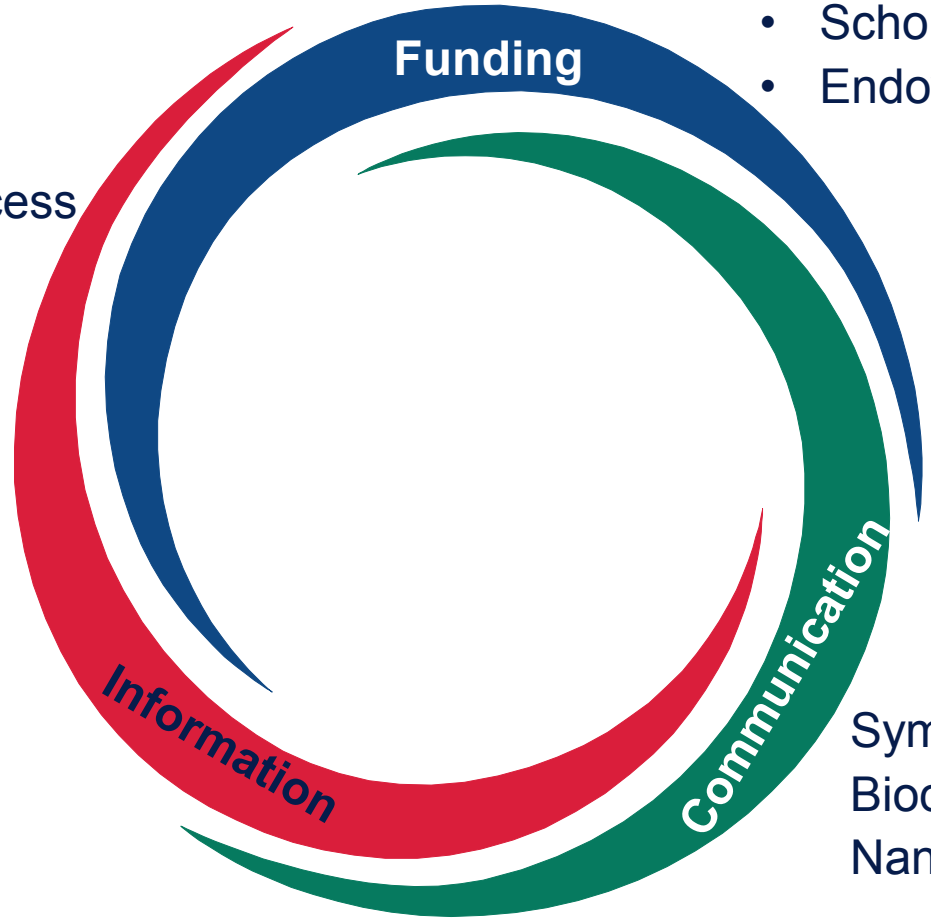

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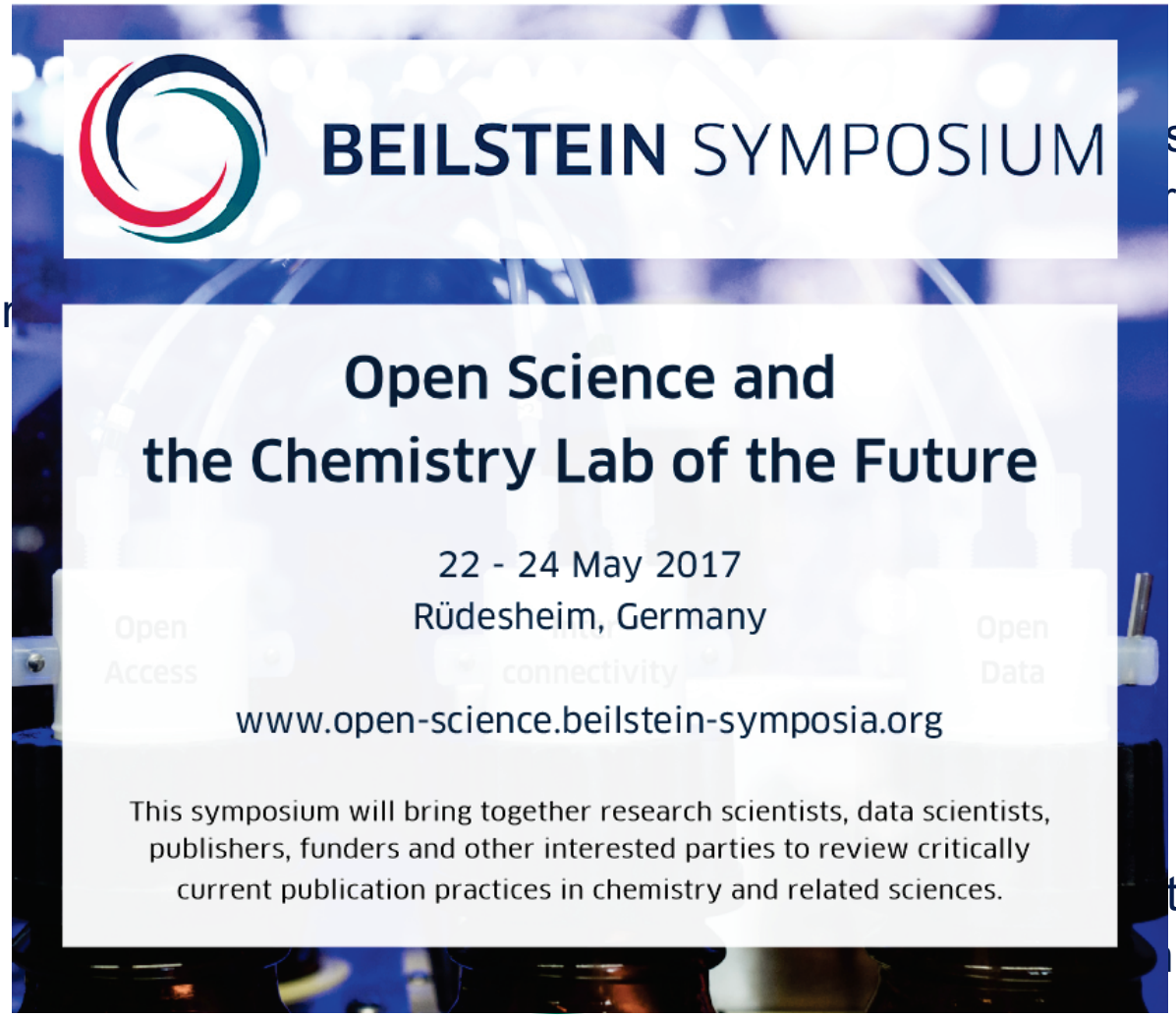
Symposia:
Biochemistry, Org. Chem.
Nano Tech., …

Beilstein-Institut

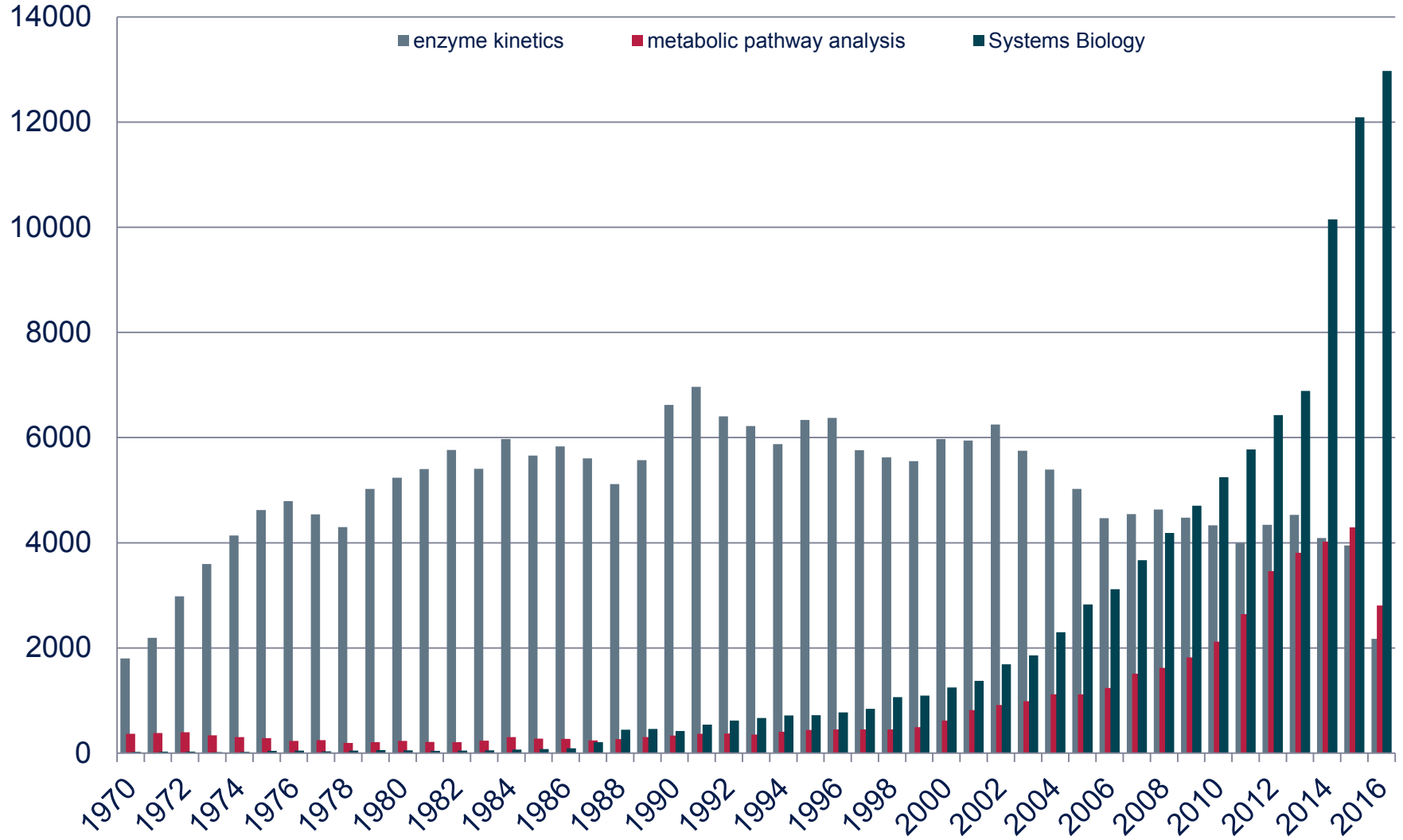


- Platinum Oper
  Journals
- Beilstein TV
- STRENDA
- MIRAGE

s
rofessorships

try, Org. Chem.
., …

Publications in enzymology



Source: PubMed (http://www.ncbi.nlm.nih.gov/pubmed), March 2017

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PLOS | MEDICINE

Essay October 2014 | Volume 11 | Issue 10 | e1001747

How to Make More Published Research True

John P. A. Ioannidis[1,2,3,4]*

1 Meta-Research Innovation Center at Stanford (METRICS), Stanford University, Stanford, California, United States of America, **2** Department of Medicine, Stanford Prevention Research Center, Stanford, California, United States of America, **3** Department of Health Research an California, United States of America, **4** Department of Statistics, Stanford University School of Humanities and

NATURE CELL BIOLOGY VOLUME 10 | NUMBER 10 | OCTOBER 2008

commentary

The challenges of integrating multi-omic data sets

Bernhard Palsson & Karsten Zengler

The capability to generate multi-omic data sets raises the issue of resource allocation for data generation versus data curation and integration. The initial experience of researchers shows that the effort required for the latter can be much greater than that for the former.

PeerJ

On the reproducibility of science: unique identification of research resources in the biomedical literature

Nicole A. Vasilevsky[1], Matthew H. Brush[1], Holly Paddock[2], Laura Ponting[3], Shreejoy J. Tripathy[4], Gregory M. LaRocca[4] and Melissa A. Haendel[1]

PeerJ 1:e148; DOI 10.7717/peerj.148

Survey in SABIO-RK: Missing and imprecise information in publications

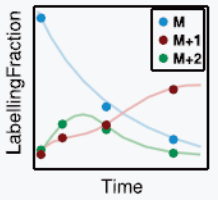
no indication of UniProtKB AC	85%
no indication of temperature	12%
"room temperature"	6%
incomplete biochemical reactions (missing products)	14%
no standard units for concentrations of compounds	20%
experimental conditions in references	10%
inconsistent experimental conditions within the publication	6%

as for September 2013

Insight into the issues

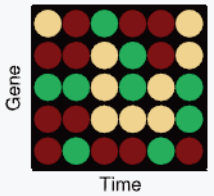
Flux Measurements

- Nutrient uptake rates
- ^{13}C-labelling (steady-state and dynamic)



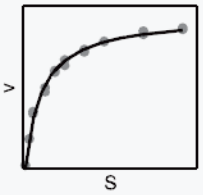
Enzyme Concentrations

- Quantititative proteomics
- Qualitative proteomics (ΔE_0)
- Expression data (ΔE_0)



Kinetic Parameters

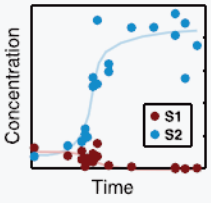
- *In vitro* assays (databases)
- BiaCore
- Existing models
- Structural calculations



$$v(S,\vec{p}) = \frac{E_0 \cdot k_{\mathrm{cat}} \cdot S}{K_{\mathrm{m}} + S}$$

Substrate Concentrations

- Metabolomics (steady-state and dynamic)
- Proteomics for signaling systems



Tummler et al. (2014) *FEBS J.* **281**:549-571

STandards for Reporting ENzymology DAta

STRENDA

founded in 2003 and supported by the Beilstein-Institut
www.beilstein-strenda.org

Richard N. Armstrong,
Amos Bairoch,
Barbara M. Bakker,
Athel Cornish-Bowden,
Paul F. Fitzpatrick,
Peter Halling,
Thomas S. Leyh,
Claire O'Donovan,

Frank M. Raushel,
Johann M. Rohwer,
Santiago Schnell
Dietmar Schomburg,
Neil Swainston,
Ming-Daw Tsai,
Roland Wohlgemuth,
Carsten Kettner

Standards for Reporting ENzymology DAta

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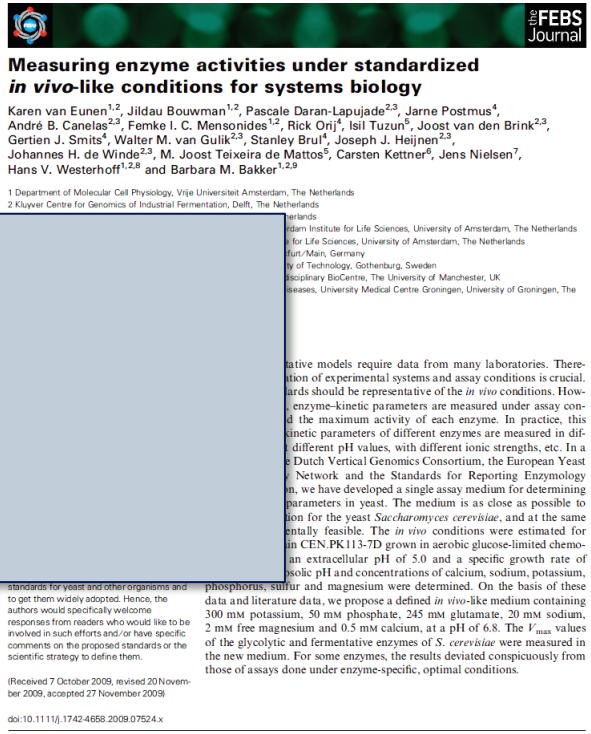

the FEBS Journal

Measuring enzyme activities under standardized *in vivo*-like conditions for systems biology

Karen van Eunen[1,2], Jildau Bouwman[1,2], Pascale Daran-Lapujade[2,3], Jarne Postmus[4], André B. Canelas[2,3], Femke I. C. Mensonides[1,2], Rick Orij[4], Isil Tuzun[5], Joost van den Brink[2,3], Gertien J. Smits[4], Walter M. van Gulik[2,3], Stanley Brul[4], Joseph J. Heijnen[2,3], Johannes H. de Winde[2,3], M. Joost Teixeira de Mattos[5], Carsten Kettner[6], Jens Nielsen[7], Hans V. Westerhoff[1,2,8] and Barbara M. Bakker[1,2,9]

1 Department of Molecular Cell Physiology, Vrije Universiteit Amsterdam, The Netherlands
2 Kluyver Centre for Genomics of Industrial Fermentation, Delft, The Netherlands
...erlands
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... for Life Sciences, University of Amsterdam, The Netherlands
...furt/Main, Germany
...y of Technology, Gothenburg, Sweden
...disciplinary BioCentre, The University of Manchester, UK
...seases, University Medical Centre Groningen, University of Groningen, The

...tative models require data from many laboratories. There-
...tion of experimental systems and assay conditions is crucial.
...ards should be representative of the *in vivo* conditions. How-
..., enzyme–kinetic parameters are measured under assay con-
...d the maximum activity of each enzyme. In practice, this
...kinetic parameters of different enzymes are measured in dif-
... different pH values, with different ionic strengths, etc. In a
...e Dutch Vertical Genomics Consortium, the European Yeast
... Network and the Standards for Reporting Enzymology
...n, we have developed a single assay medium for determining
...parameters in yeast. The medium is as close as possible to
...tion for the yeast *Saccharomyces cerevisiae*, and at the same
...entally feasible. The *in vivo* conditions were estimated for
...in CEN.PK113-7D grown in aerobic glucose-limited chemo-
... an extracellular pH of 5.0 and a specific growth rate of
...osolic pH and concentrations of calcium, sodium, potassium,
standards for yeast and other organisms and to get them widely adopted. Hence, the authors would specifically welcome responses from readers who would like to be involved in such efforts and/or have specific comments on the proposed standards or the scientific strategy to define them.

phosphorus, sulfur and magnesium were determined. On the basis of these data and literature data, we propose a defined *in vivo*-like medium containing 300 mM potassium, 50 mM phosphate, 245 mM glutamate, 20 mM sodium, 2 mM free magnesium and 0.5 mM calcium, at a pH of 6.8. The V_{max} values of the glycolytic and fermentative enzymes of *S. cerevisiae* were measured in the new medium. For some enzymes, the results deviated conspicuously from those of assays done under enzyme-specific, optimal conditions.

(Received 7 October 2009, revised 20 November 2009, accepted 27 November 2009)

doi:10.1111/j.1742-4658.2009.07524.x

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Missions:

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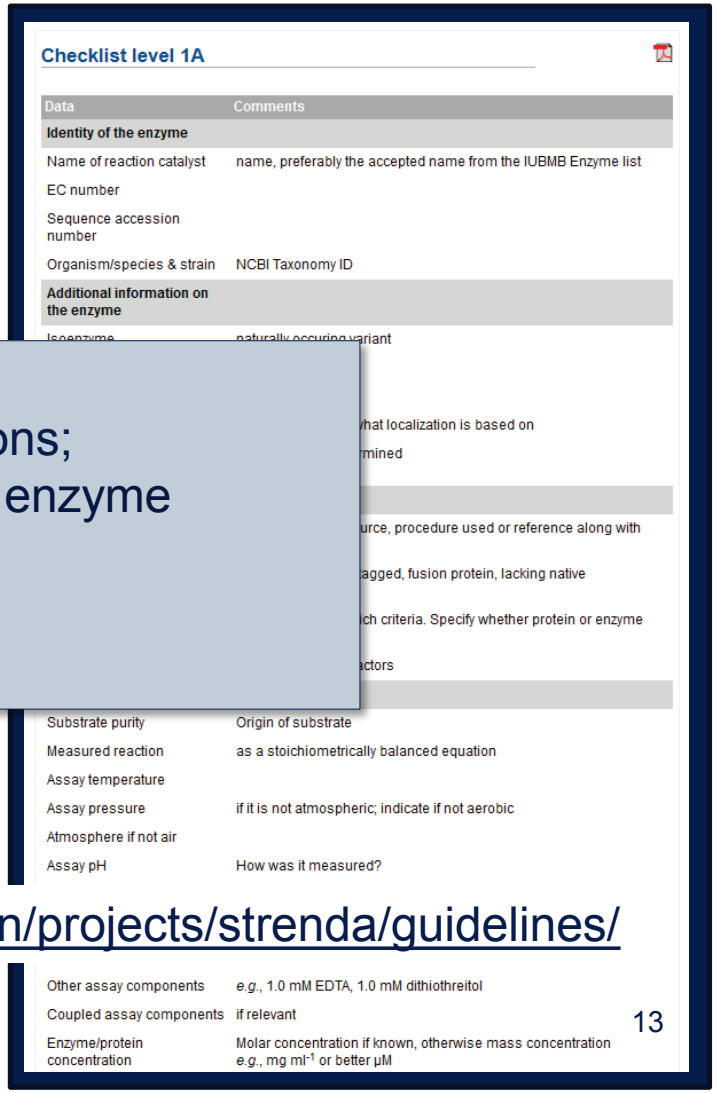
(2) Definition of minimum information for reporting enzyme functional data (STRENDA Guidelines);



Checklist level 1A

Data	Comments
Identity of the enzyme	
Name of reaction catalyst	name, preferably the accepted name from the IUBMB Enzyme list
EC number	
Sequence accession number	
Organism/species & strain	NCBI Taxonomy ID
Additional information on the enzyme	
Isoenzyme	naturally occuring variant
	hat localization is based on
	rmined
	urce, procedure used or reference along with
	agged, fusion protein, lacking native
	ch criteria. Specify whether protein or enzyme
	ctors
Substrate purity	Origin of substrate
Measured reaction	as a stoichiometrically balanced equation
Assay temperature	
Assay pressure	if it is not atmospheric; indicate if not aerobic
Atmosphere if not air	
Assay pH	How was it measured?
Other assay components	*e.g.*, 1.0 mM EDTA, 1.0 mM dithiothreitol
Coupled assay components	if relevant
Enzyme/protein concentration	Molar concentration if known, otherwise mass concentration *e.g.*, mg ml^{-1} or better µM

http://www.beilstein-institut.de/en/projects/strenda/guidelines/

STRENDA Guidelines highly recommended by:

ACS Catalysis
Archives in Biochemistry and Biophysics
Antimicrobial Agents and Chemotherapy
BBA (all nine sections)
Biochem. and Biophys. Res. Communications
Biochemical Journal
Biochemistry
Biophysical Chemistry
Clinical and Vaccine Immunology
eLife
FEBS Journal
Free Radical Research
Infection and Immunity
Journal of the American Chemical Society
mBio
Molecular and Cellular Biology
Proceedings of the National Academy of Sciences
The Journal of Bacteriology
The Journal of Biological Chemistry
The Journal of Virology
Trends in Biotechnology
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Free Radical Research
Infection and Immunity
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Molecular and Cellular Biology
Proceedings of the National Academy of Sciences
The Journal of Bacteriology
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…created by the community in consultation within
…demanded and appreciated by the community
…supported and recommended by journals
…included in instructions for authors

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Bosch Fawstin, http://fawstin.blogspot.de

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…who reads the instructions?

…who takes the burden to enforce authors to report in compliance with Guidelines?

…who takes the risk scaring authors?

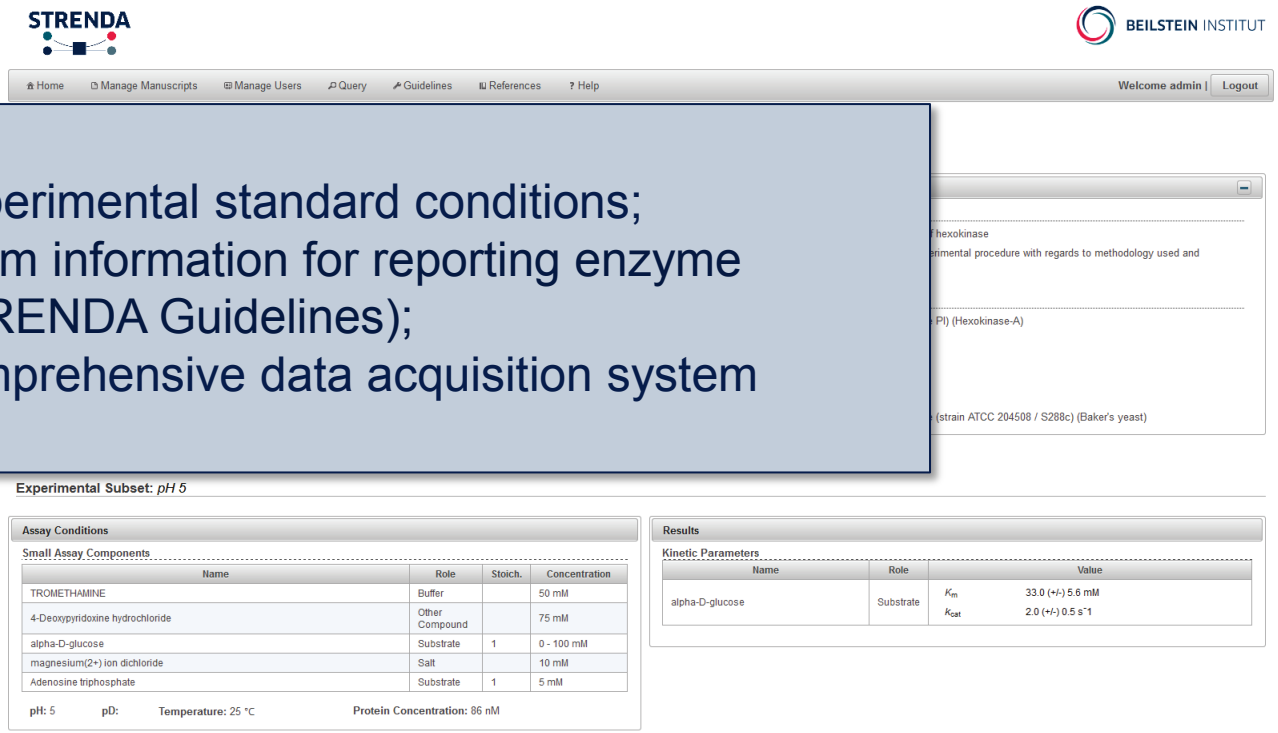
Standards for Reporting ENzymology DAta

Missions:

(1) Development of experimental standard conditions;

(2) Definition of minimum information for reporting enzyme functional data (STRENDA Guidelines);

(3) Generation of a comprehensive data acquisition system (STRENDA DB).



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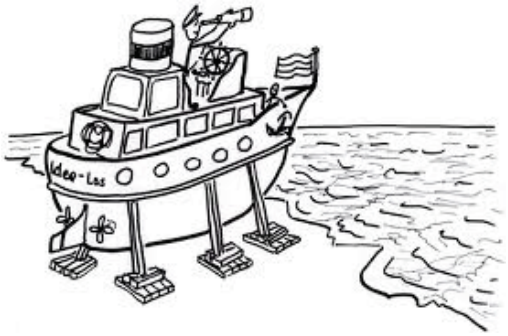
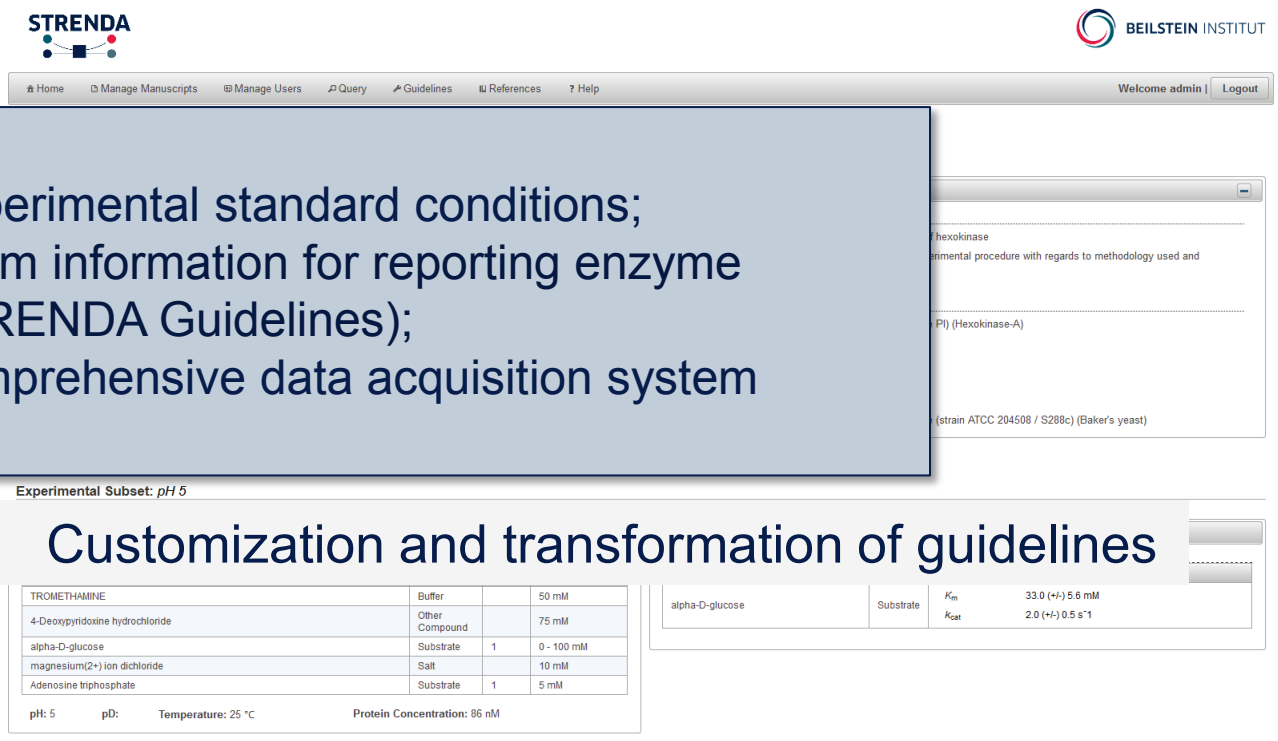
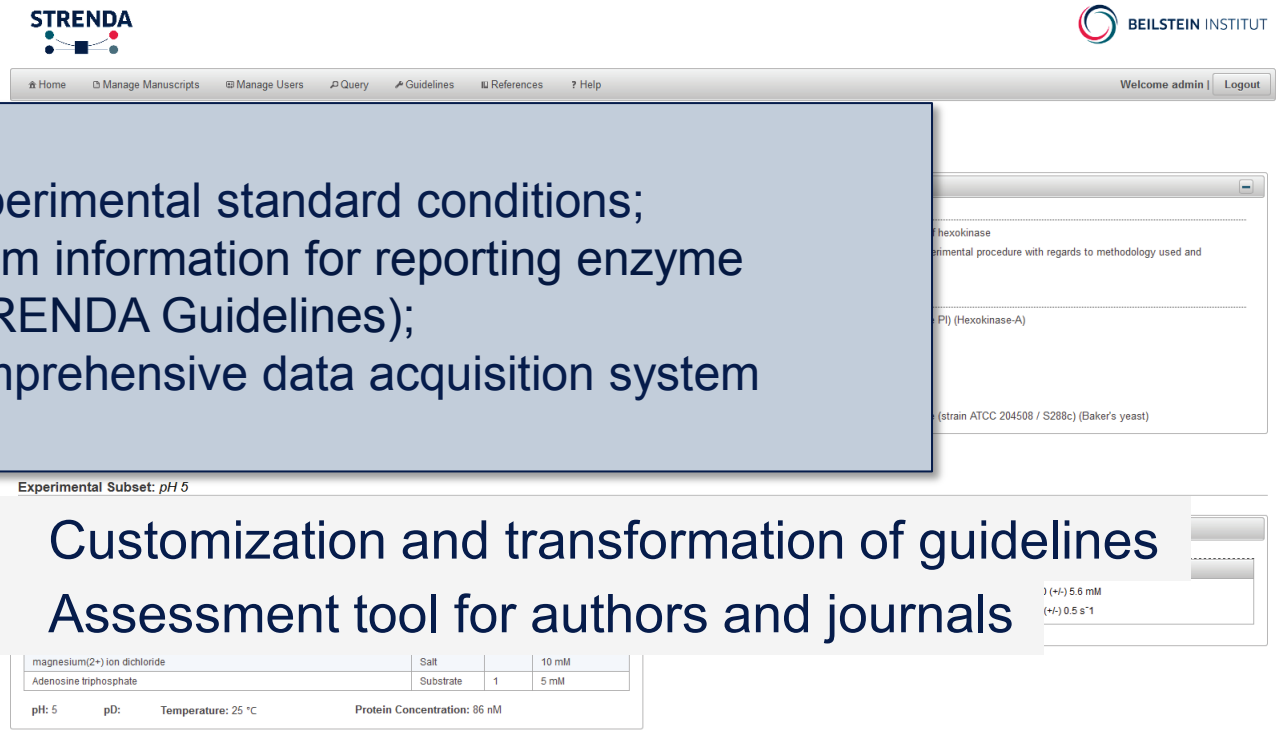




- Customization and transformation of guidelines

Standards for Reporting ENzymology DAta



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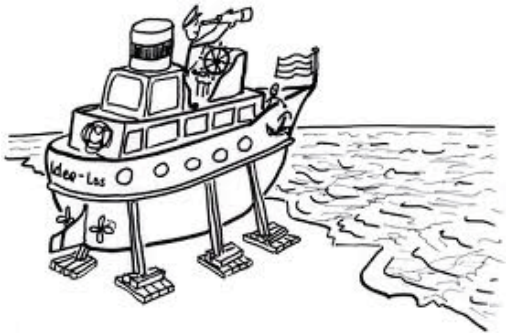
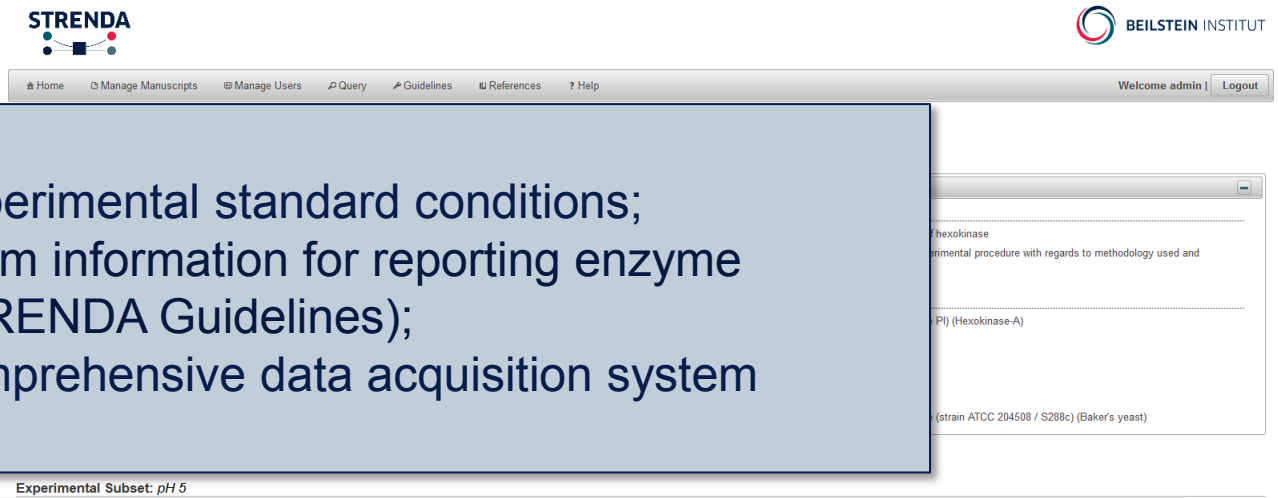


- Customization and transformation of guidelines
- Assessment tool for authors and journals

Standards for Reporting ENzymology DAta



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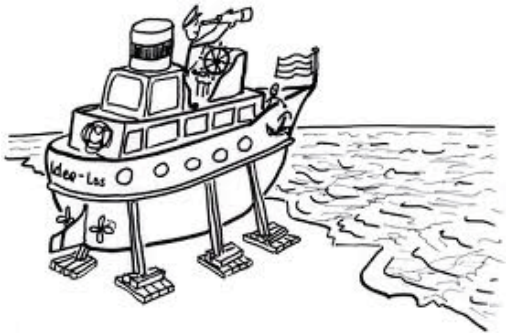

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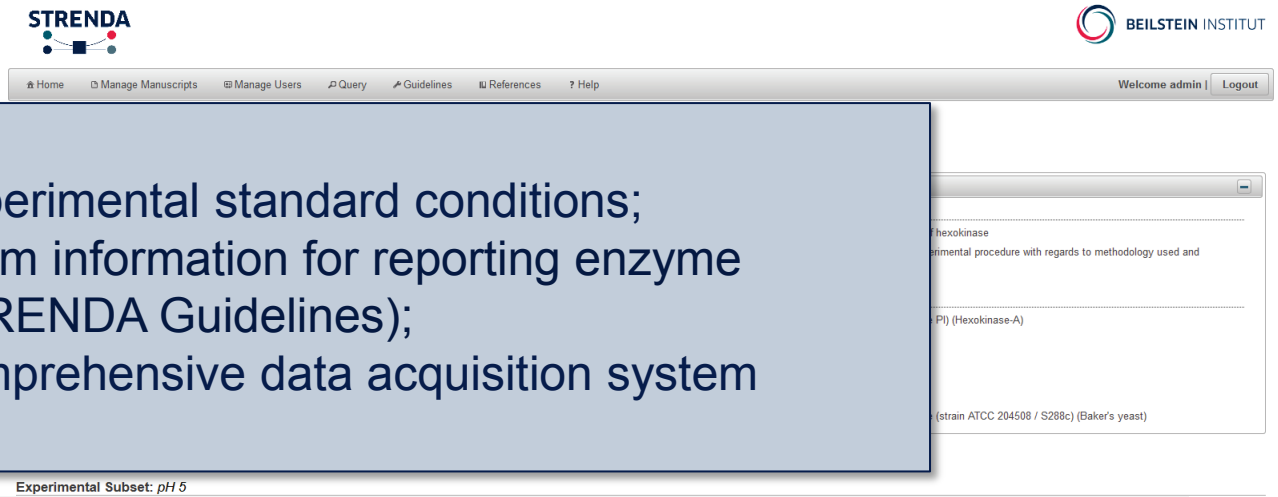

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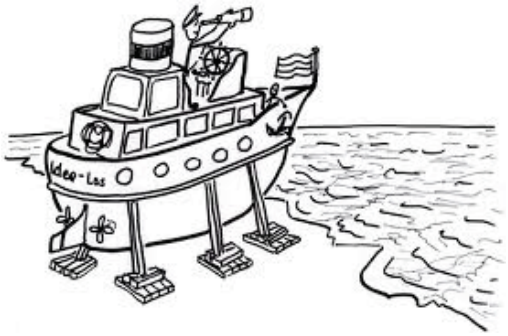

- Customization and transformation of guidelines
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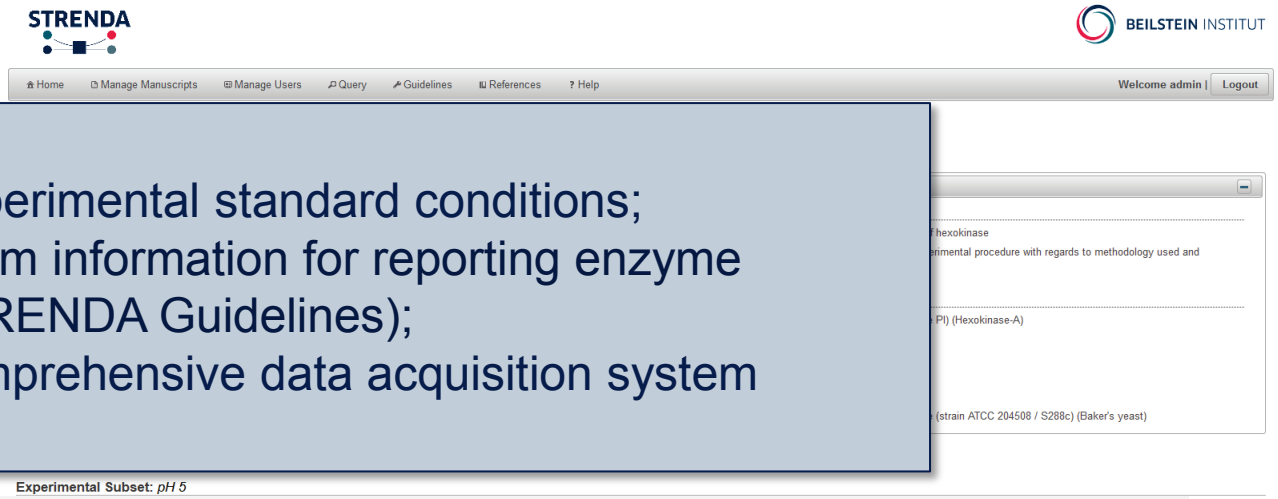
- Direct data submission by authors
- Storage of data in a free accessible data base

Standards for Reporting ENzymology DAta



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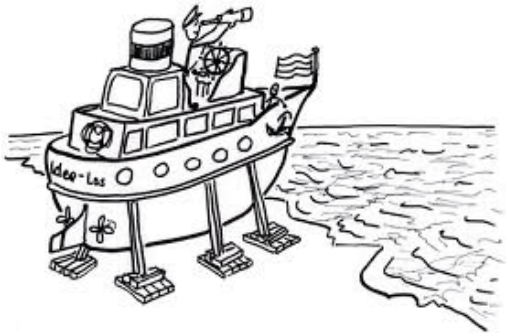
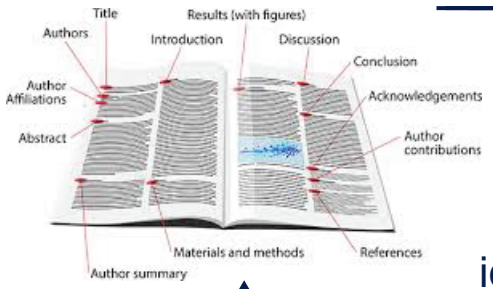
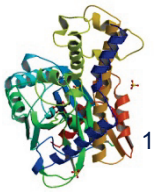


- Customization and transformation of guidelines
- Assessment tool for authors and journals
- Direct data submission by authors
- Storage of data in a free accessible data base
- STRENDA DB: the “PDB for functional enzymology”

Overview





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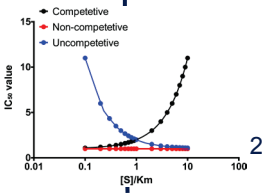


2

identifier
modifications
source
organism
reaction, assayed

methodology & techniques
assay conditions
temperature, pH

kinetics params
inhibition
activitation

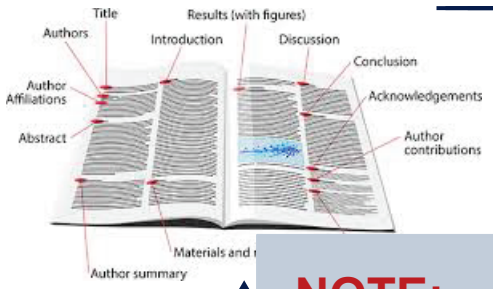
Review/ correction

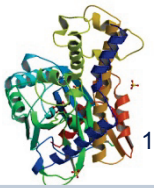
Check on compliance with STRENDA guidelines

[1] PDB: 1BDG, hexokinase

[2] Acker & Auld (2014) *Perspectives in Science* **1**(1-6):56-73.

Overview





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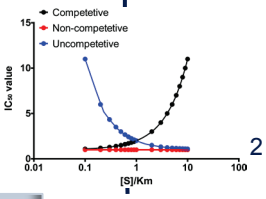


2

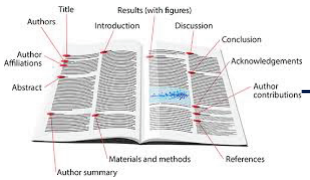
NOTE:

- not a substitute for the review process!
- emphasis on monitoring information rather than defining acceptance criteria

Check on compliance with STRENDA guidelines

[1] PDB: 1BDG, hexokinase

[2] Acker & Auld (2014) *Perspectives in Science* **1**(1-6):56-73.



Experiment

Protein data:

- Identifier
- Modifications
- Source
- Reaction

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Add Protein

Manuscript Data | Experiment

Is the protein data registered in UniProtKB? Yes | No

Search for Proteins

Search for Proteins in UniProtKB: combined | Search

Protein Description

UniProtKB AC *: P16862

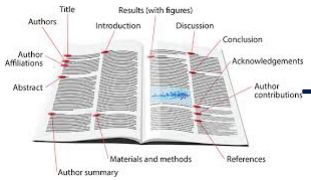
Protein Name *: ATP-dependent 6-phosphofructokinase subunit beta (ATP-dependent 6-phosphofructokinase) (ATP-PFK) (Phosphofructokinase 2) (Phosphoh

Sequence *:

```
MTVTTPFVNGTSYCTVTAYSVQSYKAAIDFYTKFLSLENRSSPDENSTLLSNDSISLKILLRPDEKINKNVEAHLKELNSITKTQDWRSHATQSLVFNTS
DILAVKDTLNAMNAPLQGYPTELFPMQLYTLDPLGNVVGVTSTKNAVSTKPTPPPAPEASAESGLSSKVHSYTDLAYRMKTTDTYPSLPKPLNRPQKAIA
VMTSGGDAPGMNSNVRAIVRSAIFKGCRAFVVMEGYEGLVRGGPEYIKEFHWEDVRGWSAEGGTNIGTARCMEFKKREGRLLGAQHLIEAGVDALIVCGG
DGSLTGADLFRSEWPSLIEELLKTNRISNEQYERMKHLNICGTVGSIDNDMSTTDATIGAYSALDRICKAIDYVEATANSHSRAFVVEVMGRNCGWLALL
AGIATSADYIFIPEKPATSSEWQDQMCDIVSKHRSRGKRTTIVVVAEGAIAADLTPISPSDVHKVLVDRLGLDTRITTLGHVQRGGTAVAYDRILATLQG
LEAVNAVLESTPDTPSPLIAVNENKIVRKPLMESVKLTKAVAEAIQAKDFKRAMSLRDTEFIEHLNNFMAINSADHNEPKLPKDKRLKIAIVNVGAPAGG
INSAVYSMATYCMSQGHRPYAIYNGWSGLARHESVRSLNWKDMLGWQSRGGSEIGTNRVTPEEADLGMIAYYFQKYEFDGLIIVGGFEAFESLHQLERAR
ESYPAFRIPMVLIPATLSNNVPGTEYSLGSDTALNALMEYCDVVKQSASSTRGRAFVVDCQGGNSGYLATYASLAVGAQVSYVPEEGISLEQLSEDIEYL
AQSFEKAEGRGRFGKLILKSTNASKALSATKLAEVITAEADGRFDAKPAYPGHVQQGGLPSPIDRTRATRMAIKAVGFIKDNQAAIAEARAAEENFNADD
KTISDTAAVVGVKGSHVVYNSIRQLYDYETEVSMRMPKVIHWQATRLIADHLVGRKRVD
```

Protein Sequence Modifications

Does the protein contain any sequence modification(s) in comparision to that of the UniProtKB entry? Yes | No | Unknown



Experiment

$Experiment_2$

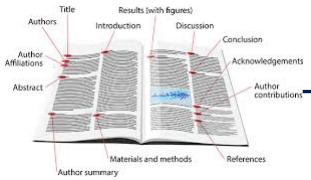
Protein data:

- Identifier
- Modifications
- Source
- Reaction

$Experiment_3$

Protein data:

- Identifier
- Modifications
- Source
- Reaction



Experiment

- Methodology & techniques
- Assay components
- Temperature
- pH

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Assay Conditions

Manuscript Data | Experiment

Assay Conditions for Experimental Subset: *2*

Small Assay Components

Role	Compound Name	ChEBI ID	PubChem CID	Stoich.	Concentration(s)	Actions
Substrate	Fructose 6-Phosphate	15946	69507	1	0.0 - 100 mM	Edit Delete
Salt	MAGNESIUM CHLORIDE	6636	5360315		20.0 mM	Edit Delete
Substrate	Adenosine triphosphate	30616	5957	1	10.0 mM	Edit Delete
Buffer	HEPES sodium salt set to pH 7.5 with HCl	46758	2724248		75.0 mM	Edit Delete
Salt	potassium chloride	32588	4873		150.0 mM	Edit Delete

Please create an entry in this table for every compound added to the assay mixture (except water, which may be taken to be the solvent unless shown otherwise).

Add component

Macromolecular Components

Role	Class	Compound Name	Database used	Identifier	Stoich.	Concentration(s)	Actions
No records found.							

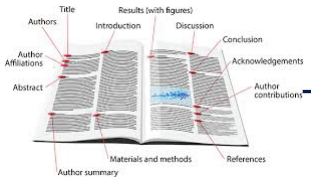
Please create an entry in this table for every compound added to the assay mixture (except water, which may be taken to be the solvent unless shown otherwise).

Add component

Concentration of the assayed protein

ATP-dependent 6-phosphofructokinase subunit beta (ATP-dependent 6-phosphofructokinase) (ATP-PFK) (Phosphofructokinase 2) (Phosphohexokinase) * 20.0 mg of pure protein ml^{-1}

How was the protein concentration measured? * optical study according to ABC



Experiment → Assay Conditions → Results

- Initial kinetics
- Inhibition
- Activation

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Edit Kinetic Parameter

Manuscript Data

Title	ATP-dependent 6-phosphofructokinase subunit beta of yeast
Author Names	Alpha B, Gamma D and Doe J
Status	open
User	ckettner
Creation Date	Feb 22, 2016
Last Work Date	Mar 7, 2016

Experiment

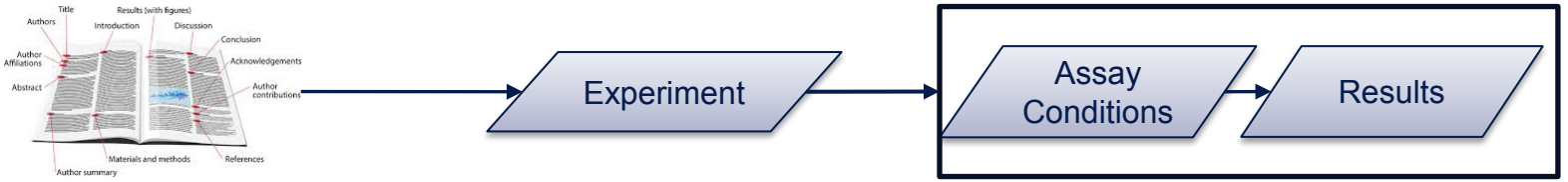
Experiment	
Description	Native PFK
Methodology	activity studied according to the methodology published by Duden K et al. (1995), J. Biochemistry.
Protein	
Protein Name	ATP-dependent 6-phosphofructokinase subunit beta (ATP-dependent 6-phosphofructokinase) (ATP-PFK) (Phosphofructokinase 2) (Phosphohexokinase)
UniProtKB AC	P16862
EC Number	2.7.1.11
Sequence modifications	no
PTM	unknown
Organism	Saccharomyces cerevisiae (strain ATCC 204508 / S288c) (Baker's yeast)

Kinetic parameters for Substrate: *Fructose 6-Phosphate*

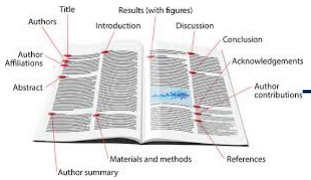
Fill in only those parameters you have obtained. Please do not enter values of those you are uncertain. You need to enter at least one value.

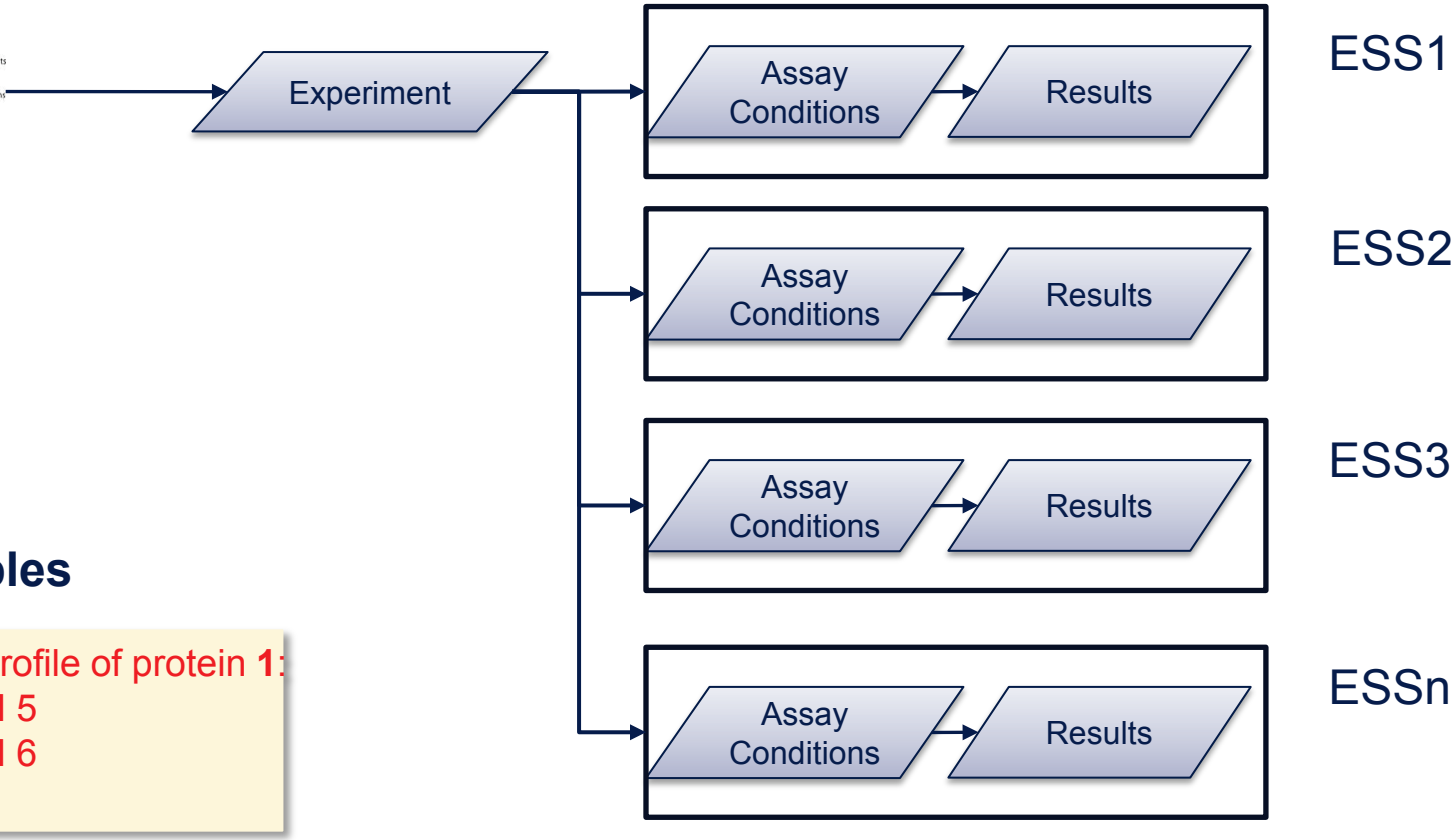
		(+/-)		
K_m	3e-7	(+/-)	2.5e-8	M
k_{cat}	1500	(+/-)	32	s^{-1}
V		(+/-)		mM min^{-1}
k_{cat}/K_m		(+/-)		M^{-1} s^{-1}
V/K_m		(+/-)		s^{-1}

Cancel | Save



Experimental Subset (ESS)

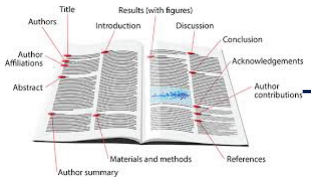




Examples

e.g. pH profile of protein **1**:
ESS_1: pH 5
ESS_2: pH 6
…

e.g. Temp. profile of protein **1**:
ESS_1 @ 15 °C
ESS_2 @ 20 °C
…



Experiment

ESS1
Assay Conditions
Results

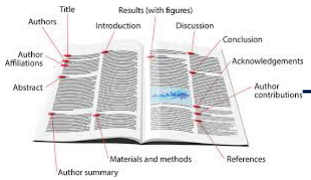
ESS2
Assay Conditions
Results

ESS3
Assay Conditions
Results

ESSn
Assay Conditions
Results

SRN/ DOI

non-public



Experiment

Assay Conditions → Results

Assay Conditions → Results

Assay Conditions → Results

Assay Conditions → Results

SRN/ DOI

public

PMID

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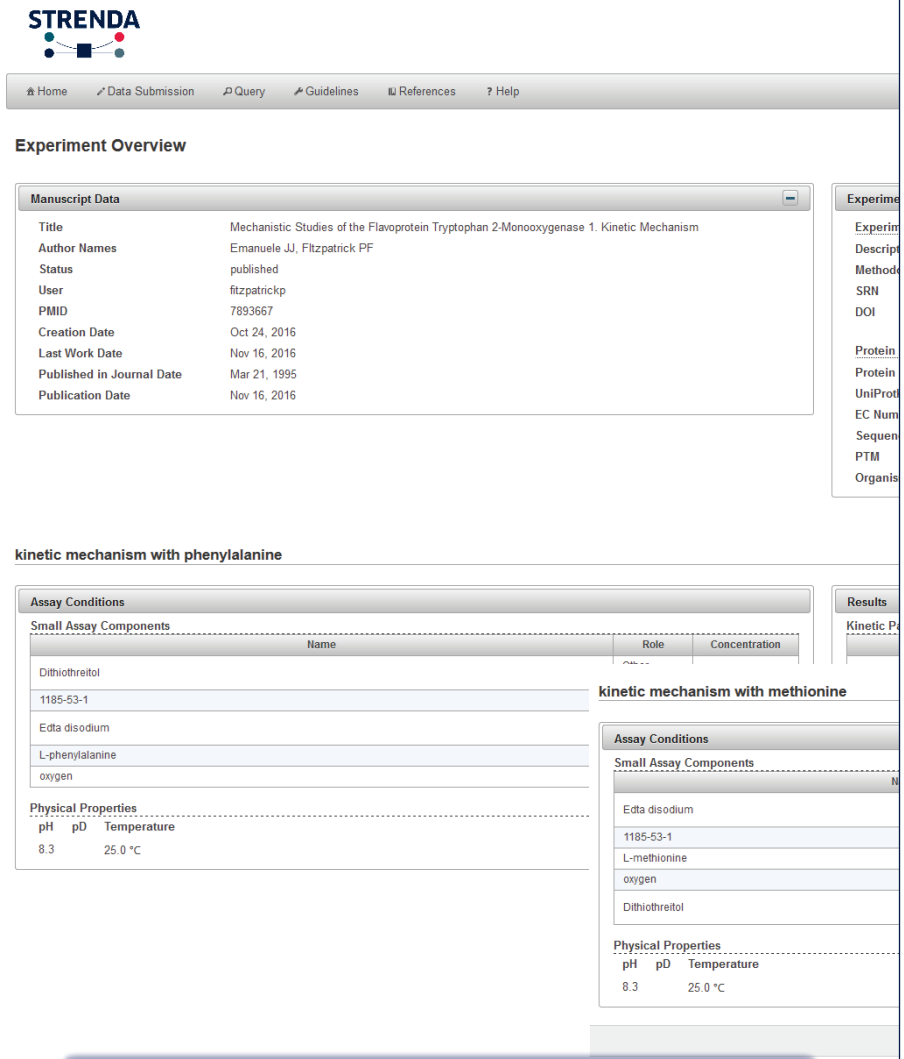
STRENDA DB: Data Overview



STRENDA DB

Experimental data fact sheet

This document provides all functional enzyme data that were obtained under the given experimental conditions, entered into STRENDA DB and assigned to the unambiguous SRN shown in the first line. This document can be submitted together with the corresponding manuscript to a journal at one's own option.

Experiment Title	Kinetic mechanism of tryptophan 2-monooxygenase with phenylalanine
Strenda ID	WZOV5O
DOI	10.22011/strenda_db.WZOV5O
Manuscript Title	Mechanistic Studies of the Flavoprotein Tryptophan 2-Monooxygenase 1. Kinetic Mechanism
Authors	Emanuele JJ, Fltzpatrick PF
Methodology	Continuous assay with oxygen electrode

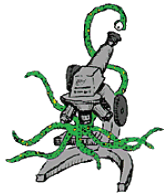
Protein

Protein Description

Is the protein data registered in UniProtKB?	yes
UniProtKB AC	P06617
Protein Name	Tryptophan 2-monooxygenase
Sequence	MYDHFNSPSIDILYDYGPFLKKCEMTGGIGSYSAGTPTPRVAIVGAGISGLVAATELLR AGVKDVVLYESRDRIGGRVWSQVFDQTRPRYIAEMGAMRFPPSATGLFHYLKKFGISTS TTFPDPGVVDTELHYRGKRYHWPAGKKPPELFRRVYEGWQSLLSEGYLLEGGSLVAPLD ITAMLKSGRLEEAAIAWQGWLNVFRDCSFYNAIVCIFTGRHPPGGDRWARPEDFELFGS LGIGSGGFLPVFQAGFTEILRMVINGYQSDQRLIPDGISSLAARLADQSFDGKALRDRV

https://www.strenda-db.org

Traditional publication process

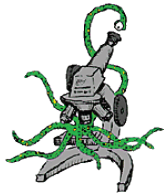


experiment

writing

submit manuscript

Traditional publication process



experiment

writing

submit manuscript

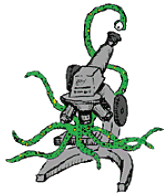
publication

editor decision

revision

editor decision

Change of a paradigm



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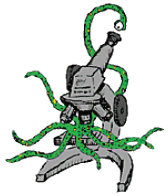
Change of a paradigm



experiment

writing

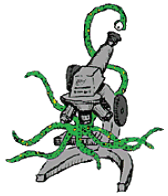
submit data

submit manuscript

novelty
plausability

editor decision

Change of a paradigm



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writing

submit data

submit manuscript

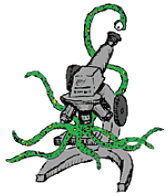
novelty
plausability

validity
reproducibility

revision

editor decision

Change of a paradigm



experiment

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novelty
plausability

validity
reproducibility

publication

editor decision

revision

editor decision

Successes & Attempts

Successes & Attempts

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