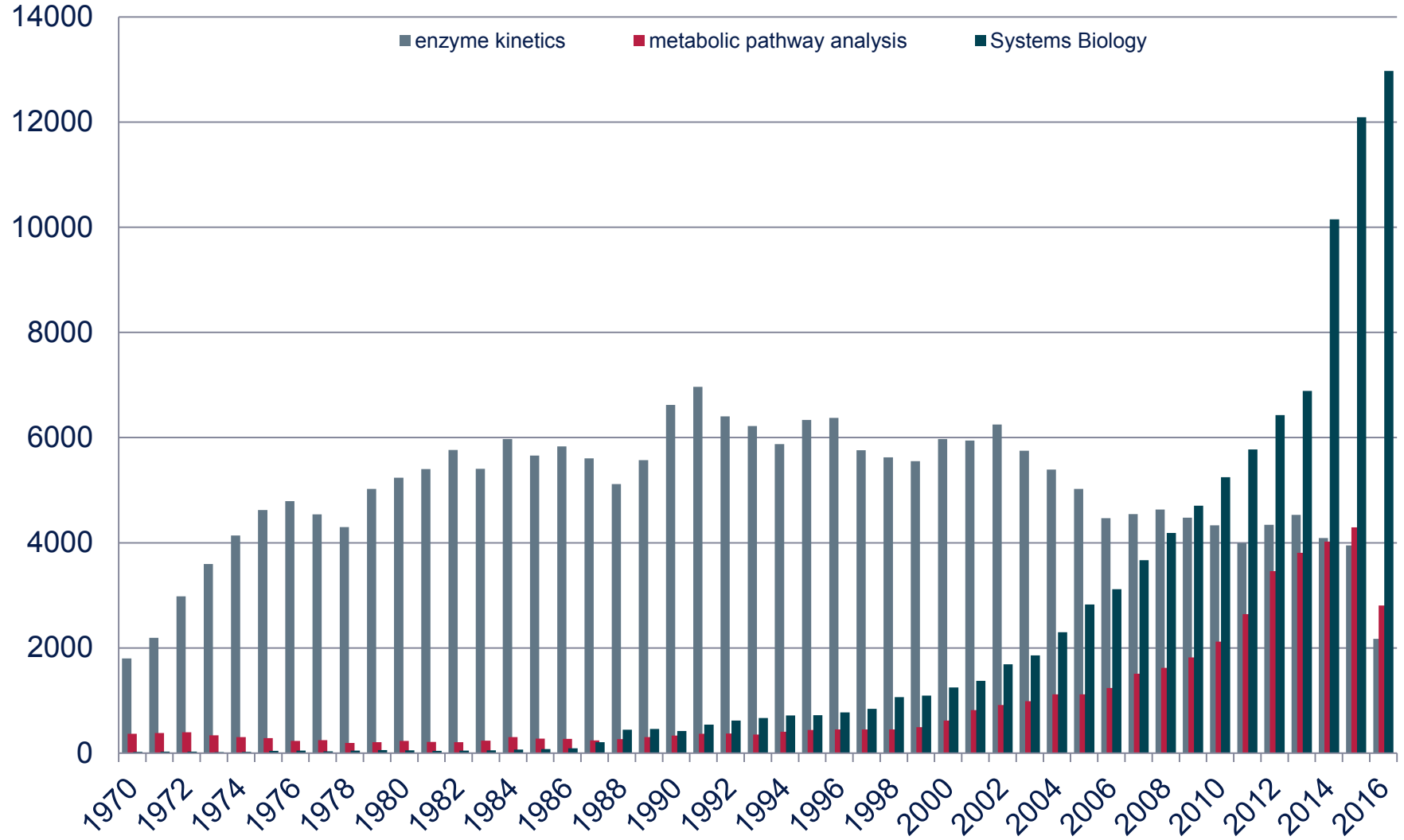
CARSTEN KETTNER

STRENDA DB:
THE PDB FOR ENZYME FUNCTION DATA?

OPEN SCIENCE DAYS 2017
BERLIN
16 & 17 OCTOBER 2017

BEILSTEIN INSTITUT

Publications in enzymology



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

Is this information useful?

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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

Missing and imprecise information …on the assay conditions…

no indication of UniProtKB AC	85%
Missing enzyme concentration	63%
no indication of temperature	12%
"room temperature"	6%
incomplete biochemical reactions (missing substrates/ products)	14%
no standard units for concentrations of compounds	20%
experimental conditions in references	10%
inconsistent experimental conditions within the publication	6%

Survey in SABIO-RK, as for September 2017

EDITORIAL

Journals unite for reproducibility

Science, Nov. 2014, 346(6210)

PERSPECTIVE

doi:10.1038/nature11556

A call for transp… optim… precli…

Story C. Landis[1], S…
Robert B. Darnell[8], …
Robert M. Golub[13], …
John Huguenard[18], …
Malcolm R. Macleod…
John D. Porter[1], Osv…

Meeting in 2014:

„…scientific journals are standing together in their conviction that reproducibility and transparency are important issues…"

Marcia McNutt, *Science*, Nov. 2014 346(6210)

…Reporting Preclinical

The signatories represent journals that publish preclinical biological research – an area of research that encompasses both exploratory studies and hypothesis-testing studies, with many different designs. The reproducibility of these studies is expected to vary. The journals agree to adhere to the following principles with the aim of facilitating the interpretation and repetition of experiments as they have been conducted in the published study. These measures and principles do not obviate the need for replication and reproduction in subsequent investigations to establish the robustness of published results across multiple biological systems.

Background

NIH held a joint workshop in June 2014 with the Nature Publishing Group and Science on the issue of reproducibility and rigor of research findings, with journal editors representing over 30 basic/preclinical science journals in which NIH-funded investigators have most often published. The workshop focused on the common opportunities in the scientific publishing arena to

http://www.nih.gov/about/reporting-preclinical-research.htm

STandards for Reporting ENzymology DAta

STRENDA

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

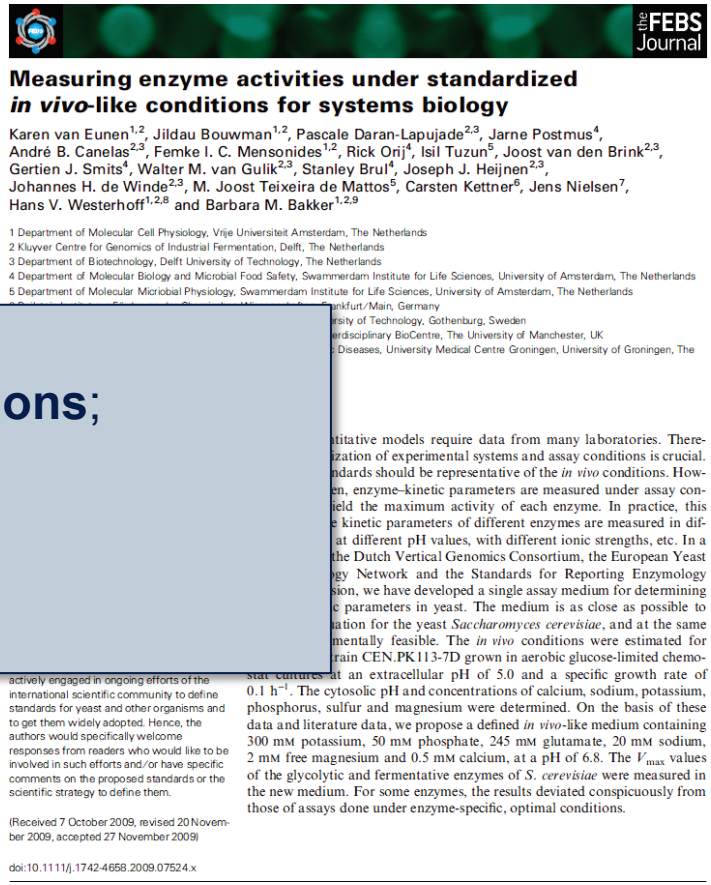
Barbara M. Bakker,
Antonio Baici,
Athel Cornish-Bowden,
Paul F. Fitzpatrick,
Peter Halling,
Thomas S. Leyh,
Claire O'Donovan,
Frank M. Raushel

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

STRENDA

Standards for Reporting ENzymology DAta

Mission:
1. Development of experimental standard conditions;



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
3 Department of Biotechnology, Delft University of Technology, The Netherlands
4 Department of Molecular Biology and Microbial Food Safety, Swammerdam Institute for Life Sciences, University of Amsterdam, The Netherlands
5 Department of Molecular Microbial Physiology, Swammerdam Institute for Life Sciences, University of Amsterdam, The Netherlands
...ankfurt/Main, Germany
...rsity of Technology, Gothenburg, Sweden
...erdisciplinary BioCentre, The University of Manchester, UK
... Diseases, University Medical Centre Groningen, University of Groningen, The

...titative models require data from many laboratories. There-
...zation of experimental systems and assay conditions is crucial.
...ndards should be representative of the *in vivo* conditions. How-
...en, enzyme-kinetic parameters are measured under assay con-
...ield the maximum activity of each enzyme. In practice, this
...e kinetic parameters of different enzymes are measured in dif-
... at different pH values, with different ionic strengths, etc. In a
...the Dutch Vertical Genomics Consortium, the European Yeast
...gy Network and the Standards for Reporting Enzymology
...sion, we have developed a single assay medium for determining
...c parameters in yeast. The medium is as close as possible to
...ation for the yeast *Saccharomyces cerevisiae*, and at the same
...mentally feasible. The *in vivo* conditions were estimated for
...rain CEN.PK113-7D grown in aerobic glucose-limited chemo-
...stat cultures at an extracellular pH of 5.0 and a specific growth rate of 0.1 h^{-1}. The cytosolic pH and concentrations of calcium, sodium, potassium, 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.

actively engaged in ongoing efforts of the international scientific community to define 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.

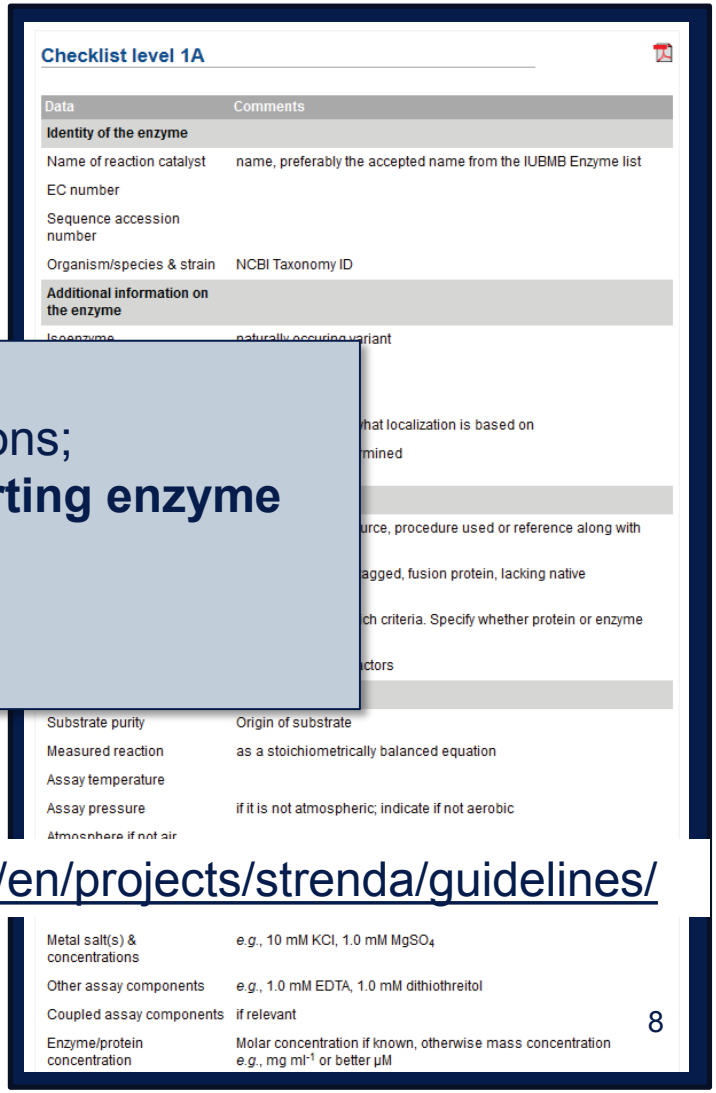
(Received 7 October 2009, revised 20 November 2009, accepted 27 November 2009)

doi:10.1111/j.1742-4658.2009.07524.x

Standards for Reporting ENzymology DAta

Mission:

1. Development of experimental standard conditions;
2. **Definition of minimum information for reporting enzyme function 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
	mined
	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	
Metal salt(s) & concentrations	*e.g.*, 10 mM KCl, 1.0 mM $MgSO_4$
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
[...]

FAIRsharing.org

PLoS Journals
BioMedCentral Journals

Beilstein J. Org. Chem.
eLife
FEBS Lett.
J. Biomed. Sci.
Nature
OMICS
Science

Standards are…

Standards are…

- … demanded and appreciated by the community
- … created by the community after internal and external consultation
- … recommended by journals
- … included in instructions for authors

Standards are…

Standards are…	… demanded and appreciated by the community
	… created by the community after internal and external consultation
	… recommended by journals
	… included in instructions for authors
In addition, they are…	… often (comprehensively) long
	… too complicated
	… for experts only

Standards are useful…

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

Standards are useful…

…BUT…

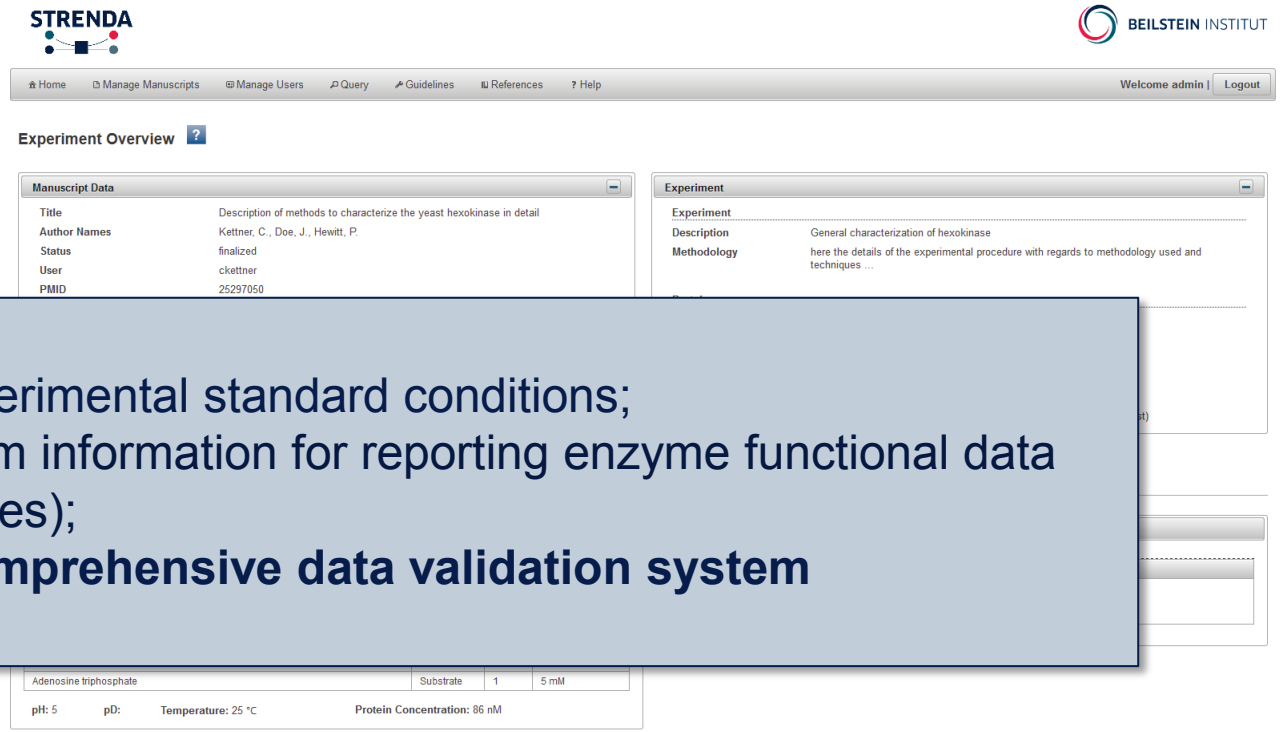
…they are disregarded since

- "nobody" reads instructions
- not consistently enforced by editors

Some prerequisites for acceptance

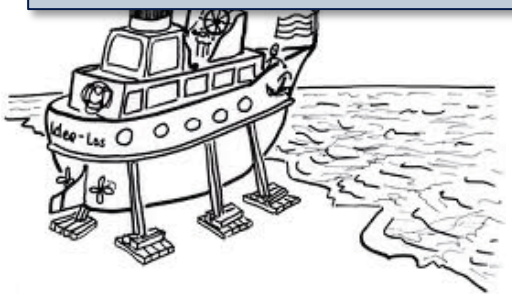
1. **Sufficiency.**	Comprehensive and relevant
2. **Practicability.**	Useful but not too burdensome
3. **Stability.**	Long-term access and support

Making standards useful



Missions:

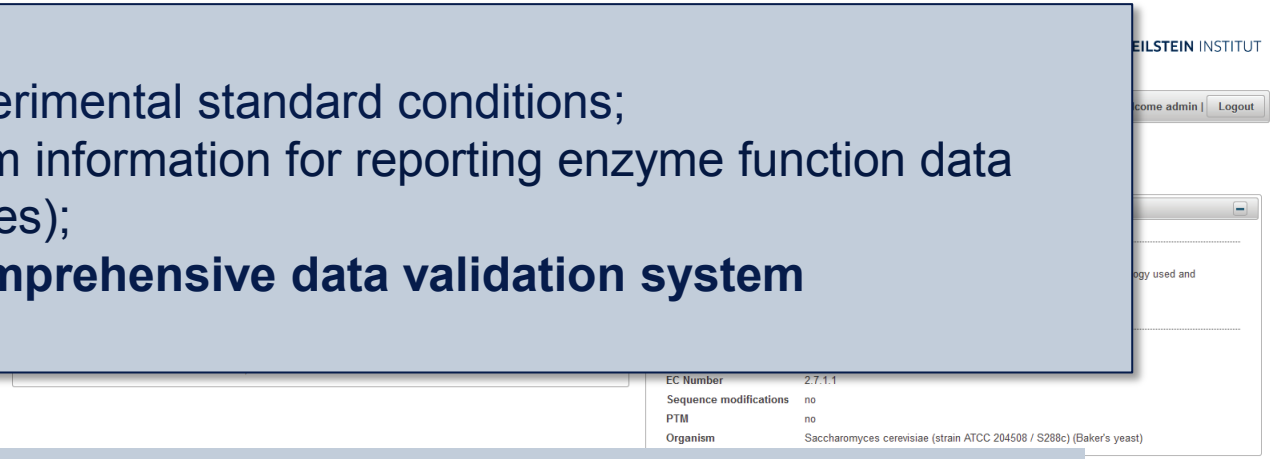
1. Development of experimental standard conditions;
2. Definition of minimum information for reporting enzyme functional data (STRENDA Guidelines);
3. **Generation of a comprehensive data validation system (STRENDA DB).**



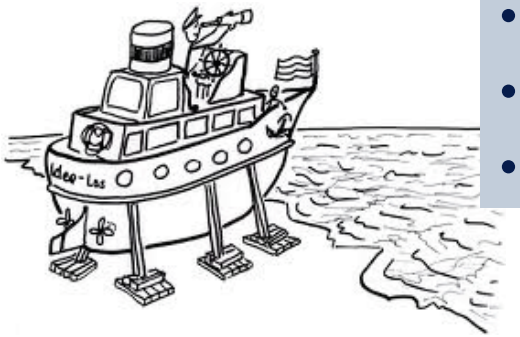
Making standards applicable

Mission:

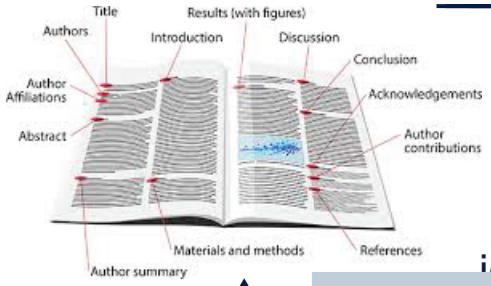
1. Development of experimental standard conditions;
2. Definition of minimum information for reporting enzyme function data (STRENDA Guidelines);
3. **Generation of a comprehensive data validation system (STRENDA DB).**

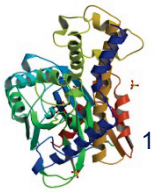


- Customize, transform and update guidelines
- Assessment tool for authors and journals
- Direct data submission by authors
- Storage of data in a freely accessible database
- STRENDA DB: the “PDB for enzyme function”



Overview





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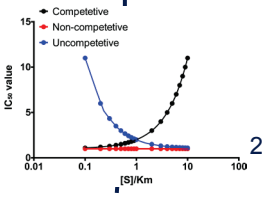


2

identifier

methodology & techniques

kinetic params

on

ation

Review
correcti

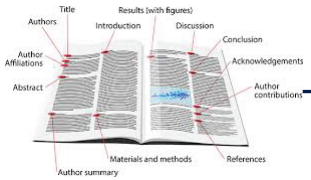
IMPORTANT:

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

Check for compliance with STRENDA guidelines

[1] PDB: 1BDG, hexokinase

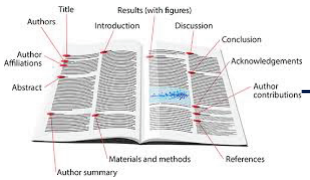
[2] Acker & Auld (2014) *Perspectives in Science* **1**(1-6):56-73.



Experiment

Definition of

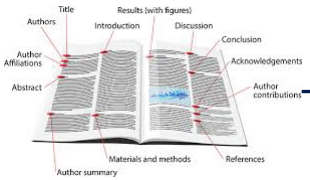
- Type of Experiment
- Methodology
- Techniques



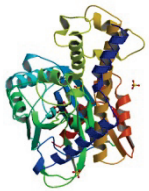
Experiment

Definition of

- Type of Experiment
- Methodology
- Techniques



Experiment



Protein data:

- Identifier
- Source
- Modifications
- 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

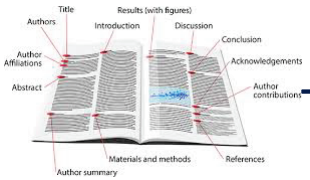
Protein Name *: ATP-dependent 6-phosphofructokinase subunit beta (ATP-dependent 6-phosphofructokinase) (ATP-PFK) (Phosphofructokinase 2) (Phosphoh

Sequence *:

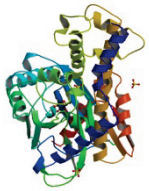
```
MTVTTPFVNGTSYCTVTAYSVQSYKAAIDFYTKFLSLENRSSPDENSTLLSNDSISLKILLRPDEKINKNVEAHLKELNSITKTQDWRSHATQSLVFNTS
DILAVKDTLNAMNAPLQGYPTELFPMQLYTLDPLGNVVGVTSTKNAVSTKPTPPPAPEASAESGLSSKVHSYTDLAYRMKTTDTYPSLPKPLNRPQKAIA
VMTSGGDAPGMNSNVRAIVRSAIFKGCRAFVVMEGYEGLVRGGPEYIKEFHWEDVRGWSAEGGTNIGTARCMEFKKREGRLLGAQHLIEAGVDALIVCGG
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

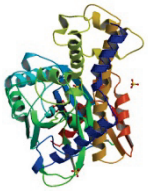


Experiment$_1$



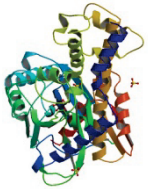
Protein data:
- Identifier
- Source
- Modifications
- Reaction

Experiment$_2$

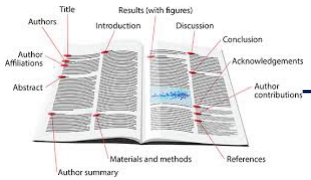


Protein data:
- Identifier
- Source
- Modifications
- Reaction

Experiment$_3$



Protein data:
- Identifier
- Source
- Modifications
- Reaction



Experiment

- 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

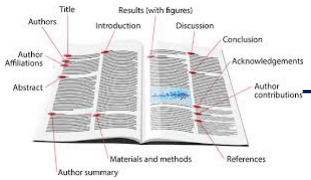
Concentration of the assayed protein

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

- Kinetic params
- 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

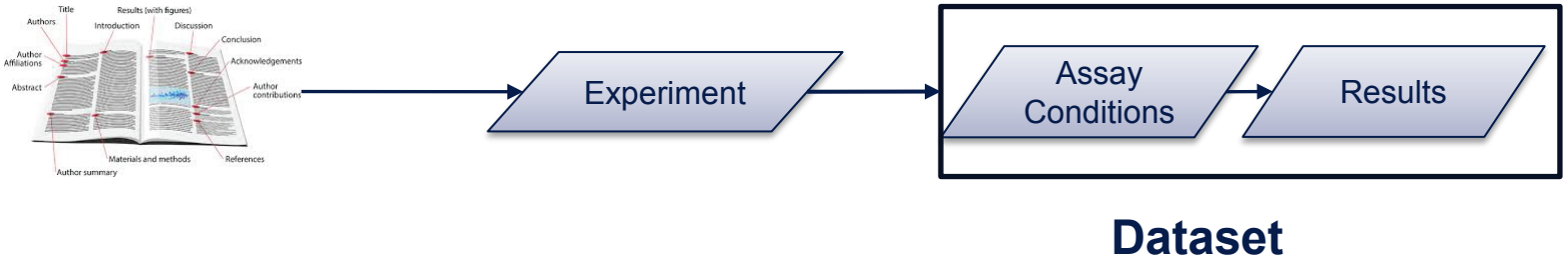
Experiment	
Description	Native PFK
Methodology	activity studied according to the methodology published by Duden K et al. (1995), J. Biochemistry.
Protein	
Protein Name	ATP-dependent 6-phosphofructokinase subunit beta (ATP-dependent 6-phosphofructokinase) (ATP-PFK) (Phosphofructokinase 2) (Phosphohexokinase)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

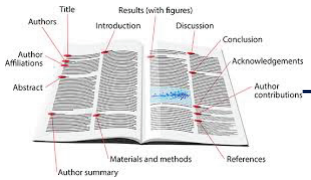
Kinetic parameters for Substrate: *Fructose 6-Phosphate*

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


Title
Authors
Author Affiliations
Abstract
Author summary
Introduction
Results (with figures)
Discussion
Conclusion
Acknowledgements
Author contributions
Materials and methods
References
Experiment
Assay Conditions
Results
Dataset



Experiment

Assay Conditions → Results — $Dataset_1$

Assay Conditions → Results — $Dataset_2$

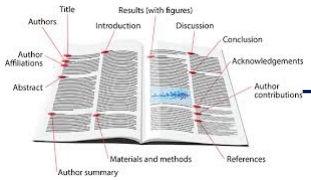
Assay Conditions → Results — $Dataset_3$

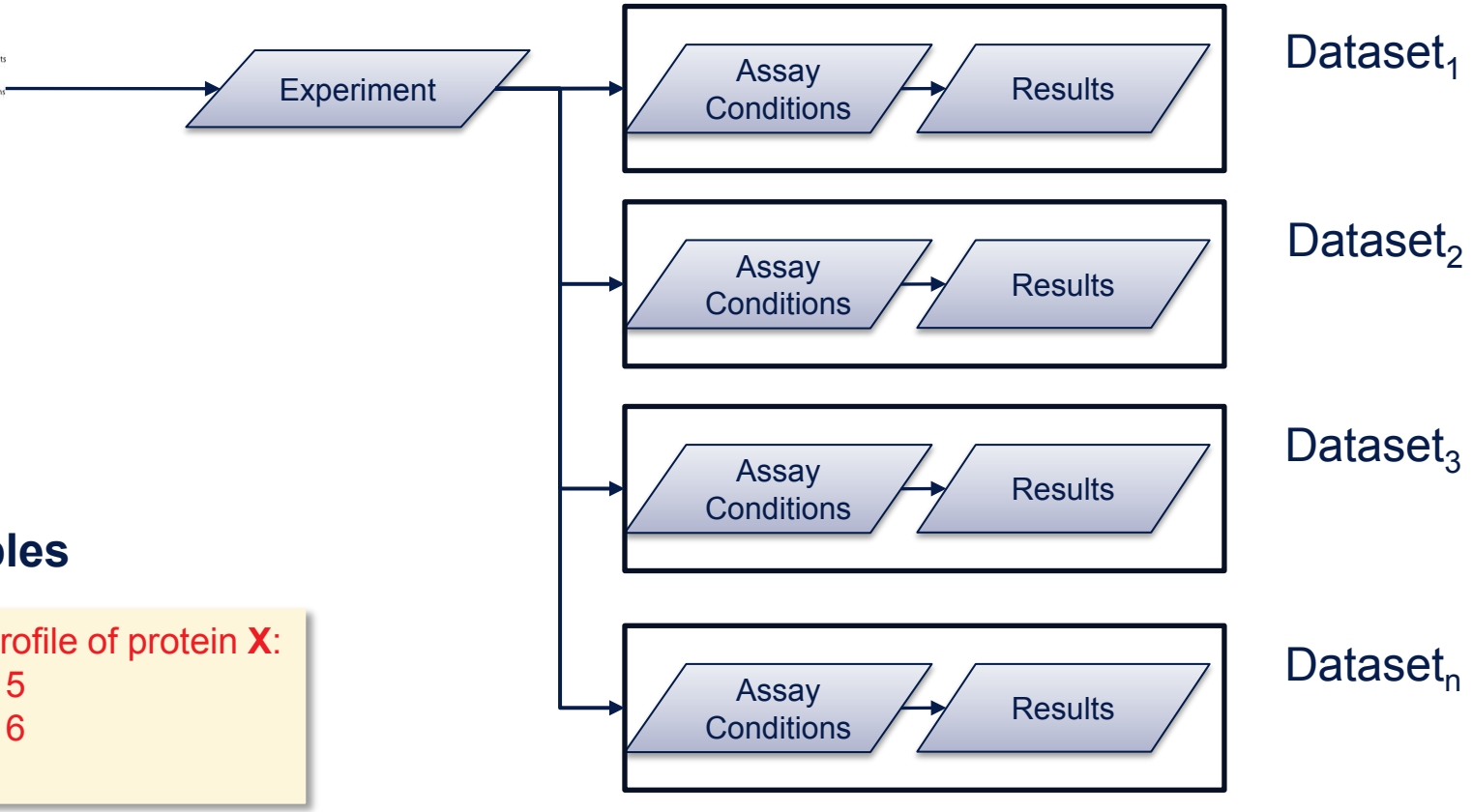
Assay Conditions → Results — $Dataset_n$

Examples

e.g. pH profile of protein **X**:
Exp_1: pH 5
Exp_2: pH 6
…

e.g. Temp. profile of protein **Y**:
Exp_1 @ 15 °C
Exp_2 @ 20 °C
…

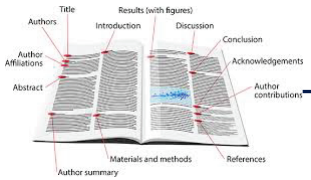




Examples

e.g. pH profile of protein **X**:
Exp$_1$: pH 5
Exp$_2$: pH 6
…

e.g. Temp. profile of protein **Y**:
Exp$_1$ @ 15 °C
Exp$_2$ @ 20 °C
…



Experiment

Dataset$_1$
Assay Conditions → Results

Dataset$_2$
Assay Conditions → Results

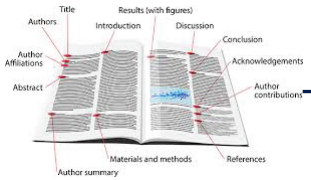
Dataset
Assay Conditions → Results

Dataset$_n$
Assay Conditions → Results

SRN/ DOI

non-public

PMID



Experiment

Dataset$_1$
Assay Conditions → Results

Dataset$_2$
Assay Conditions → Results

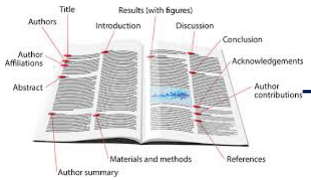
Dataset
Assay Conditions → Results

Dataset$_n$
Assay Conditions → Results

SRN/ DOI

non-public

PMID



Enzyme

Assay Conditions → Results

Assay Conditions → Results

Assay Conditions → Results

Assay Conditions → Results

SRN/ DOI

public

PMID

STRENDA DB: Data Overview

STRENDA

Home | Data Submission | Query | Guidelines | References | Help

Experiment Overview

Manuscript Data

Title	Mechanistic Studies of the Flavoprotein Tryptophan 2-Monooxygenase 1. Kinetic Mechanism
Author Names	Emanuele JJ, Fltzpatrick PF
Status	published
User	fitzpatrickp
PMID	7893667
Creation Date	Oct 24, 2016
Last Work Date	Nov 16, 2016
Published in Journal Date	Mar 21, 1995
Publication Date	Nov 16, 2016

kinetic mechanism with phenylalanine

Assay Conditions

Small Assay Components

Name
Dithiothreitol
1185-53-1
Edta disodium
L-phenylalanine
oxygen

Physical Properties

pH	pD	Temperature
8.3		25.0 °C

kinetic mechanism with methionine

Assay Conditions

Small Assay Components

Edta disodium
1185-53-1
L-methionine
oxygen
Dithiothreitol

Physical Properties

https://www.strenda-db.org

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.

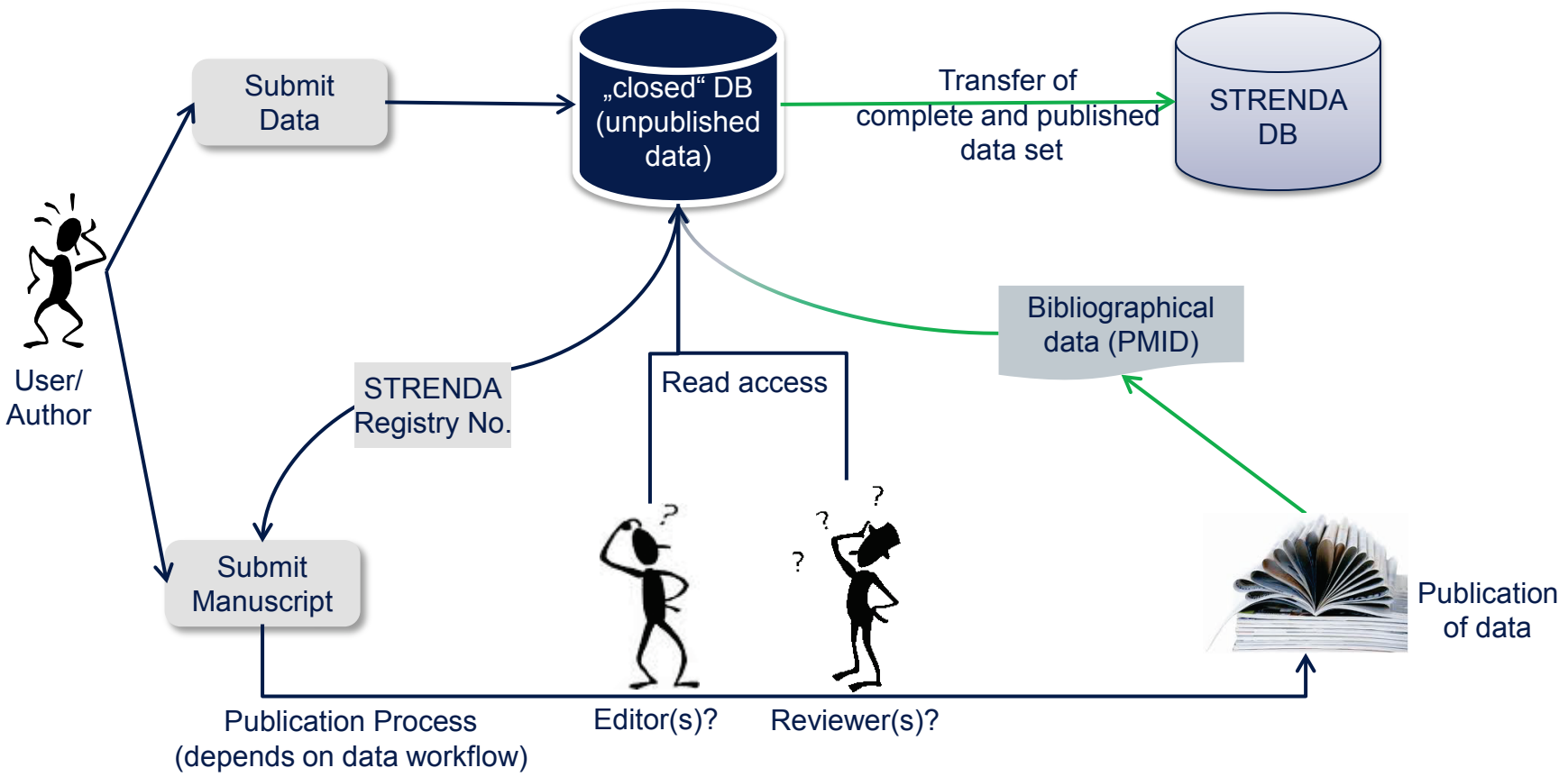
Experiment Title	Kinetic mechanism of tryptophan 2-monooxygenase with phenylalanine
Strenda ID	WZOV5O
DOI	10.22011/strenda_db.WZOV5O
Manuscript Title	Mechanistic Studies of the Flavoprotein Tryptophan 2-Monooxygenase 1. Kinetic Mechanism
Authors	Emanuele JJ, Fltzpatrick PF
Methodology	Continuous assay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

Protein

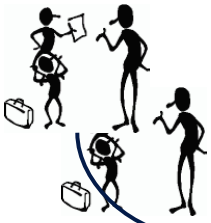
Protein Description

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

STRENDA DB: Interaction of stakeholders



STRENDA DB: Perspectives and benefits



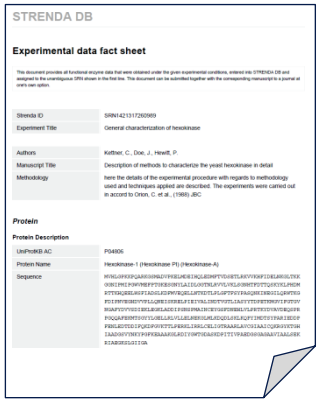
other DBs

e.g.
- BRENDA
- SABIO-RK
- …

- comparison of kinetic data
- access to assay conditions
- comprehensive information on proteins
- data summary sheet as SI

STRENDA DB

Web services (read access)



STRENDA DB

Experimental data fact sheet

- free access to data
- low burden for authors
- data input prior or during publication
- uniform structure of information

Perspectives
- LIMS
- Archive
- ELN

Successes & Progesses

Recommended by:

eLIFE

npg

BEILSTEIN JOURNAL OF ORGANIC CHEMISTRY

jbc The Journal of Biological Chemistry

PLOS

SCIENTIFIC DATA

Registered with:

re3data.org
REGISTRY OF RESEARCH DATA REPOSITORIES

OpenDOAR

OpenAIRE

Compliant with and harvested from

FAIRsharing.org
standards, databases, policies

First data coming in …

https://www.strenda-db.org

Contact: strenda@beilstein-institut.de