

Minutes of the





Meeting

September 11, 2023

Hotel Jagdschloss Niederwald Rüdesheim, Germany

by
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based on the notes of Thomas Leyh and Carsten Kettner



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January, 2024



The 19th STRENDA meeting took place on Monday, September 11, 9 am – 5 pm, at the Hotel Jagdschloss Niederwald in Rüdesheim, Germany. As some members could not travel, the meeting was hosted as a hybrid event allowing the remote members to participate and contribute to the discussions.

List of Participants

- Barbara Bakker, University Medical Center Groningen, The Netherlands
- María Luz Cardenas, CNRS-BIP, Marseille, France
- Athel Cornish-Bowden, CNRS-BIP, Marseille, France
- Robert Giessmann, Berlin
- Robert Goldberg, NIST, Gaithersburg, MA, USA (online)
- Thomas S. Leyh, The Albert-Einstein-College of Medicine, Bronx, NY, USA
- Andrew McDonald, Trinity College Dublin, Ireland
- Jürgen Pleiss, University of Stuttgart, Germany
- Frank M. Raushel, Texas A&M University, College Station, USA
- Johann Rohwer, University of Stellenbosch, South Africa
- Johann M. Rohwer, University of Stellenbosch, South Africa
- · Santiago Schnell, University of Notre Dame, IN, USA
- Hans V. Westerhoff, Universities of Amsterdam, The Netherlands
- Ulrike Wittig, Heidelberg Institute for Theoretical Studies, Germany
- Roland Wohlgemuth, Lodz University of Technology, Poland
- Carsten Kettner (co-ordination), Beilstein-Institut, Frankfurt, Germany

Unfortunately absent (with excuse)

- Paul Fitzpatrick, University of Texas Health Science Center at San Antonio, TX, USA
- Ming-Daw Tsai, Academia Sinica, Taipei, Taiwan
- Peter Halling, University of Strathclyde, Glasgow, UK



Agenda

Monday, September 11

Opening and Welcome

(Carsten Kettner)

STRENDA – **news and activities** - Overview of the latest news (Carsten Kettner)

STRENDA DB - numbers, new developments (Carsten Kettner, Andrew McDonald)

EnzymeML - status and progresses (Jürgen Pleiss)

Extending the STRENDA Guidelines – Reporting Guidelines for Biocatalysis Experiments Status

(Jürgen Pleiss, Carsten Kettner)

Recommendations for kinetic modelling

(Santiago Schnell)

Underpinning paper funding the thermodynamics

(Hans Westerhoff)

OpenTERC – **open database on thermodynamics of enzyme-catalyzed reactions** (Robert Giessmann)

General topics

no longer demand of EC numbers by journals?



STRENDA - news and activities

Withdrawals from the Commission

Meina Neumann-Schaal got another appointment and thus is not longer responsible for BRENDA. Therefore, she decided to step back but she emphasized that she will be stay in contact if the Commission asks for his advice. The Commission thanks Meina for her short engagement and for her contributions to the STRENDA project.

ACTION POINT

Carsten will contact the new representative of BRENDA.

STRENDA DB @ NFDI4Chem

NFDI4Chem is the German initiative on the establishment of National Research Data Infrastructures funded by the DFG. There are ~30 commissions each representing both entire and subdisciplines of research areas. The aim of the NFDIs is to create technological infrastructure such as standards, exchange formats, tools, ontologies etc., to extend existing databases and to educate researchers in data management. The Beilstein-Institut partners the commission for chemistry through STRENDA and MIRAGE.

STRENDA DB is appointed one of the five Core Repositories of NFDI4Chem. CK presented STRENDA DB at the Chemical Data Days in Mainz, March 2023.

Data links to Europe PMC

EuropePMC provides users with links from the abstract of the published paper to data stored in repositories and databases. The generation of this link requires the use of a specific metadata template to upload the connections of datasets and EuropePMC identifiers. This needs to be done manually as there is no API or any other automatic process available. An example, how this linking looks like, is a paper of Taylor et al. JACS, 2017, DOI:10.1021/jacs.7b04824, PMID: 28650156, PMC5629633. On EuropePMC scroll down the hit to "Data behind the article".

The linking of STRENDA DB datasets with PubMed is in progress.



Recommendations for STRENDA DB

Wiley-VCH updated its data deposition policy for all journals of European Chemical Societies that publish the following journals: *European Journal of Inorganic Chemistry, European Journal of Organic Chemistry, ChemCatChem, ChemSusChem, ChemBioChem, Chemistry Europe, ChemSystemsChem.* With this addition, more than 25 journals recommend their authors to deposit their data in STRENDA DB. And, of course, the list of journal that recommend the STRENDA Guidelines has increased by these seven journals as well.

Publication

Bob Goldberg *et al.* published their recommendations for reporting measurements of equilibrium constants of enzyme reactions in March in *Beilstein Journal of Organic Chemistry* (https://doi.org/10.3762/bjoc.19.26). This paper is considered an addendum to the STRENDA Guidelines and thus the recommendations have been kept as brief as possible.

In addition, it incorporates the recommendations made in 2011 by the International Union of Biochemistry and Molecular Biology (IUBMB),

(https://doi.org/10.1016%2Fj.bpc.2011.03.007).

ACTION POINTS

Authors: Add a short text version to the STRENDA Guidelines on the website

STRENDA DB

Overview

The current technical version is 1.3.2 (from June 7, 2023). In June, the link between STRENDA DB to UniProtKB broke as UniProt switched-off their legacy server which meant STRENDA DB searches for proteins came up blank. The RESTFul API of UniProt is now in place.

The database provides >90 datasets to the public, 20 additional datasets are going to be finalized (assignment to the publication is missing). There are some entries of doubt (no reference found, incomplete and "sloppy" data) which will be removed after another double-check. Many more new data sets just have been started but no further progress could have been observed.



When contacting the authors, these messages often remain without any replies which is a strong indication that the data sets generated are "death" ones which have been created for testing reasons. These datasets will be removed as well.

Technical Developments of STRENDA DB

(presented by Andrew McDonald)

Andrew presented a live demo of the new development where the free text field describing the methodology used in the experiment has been split into a variety of new fields including predefined pull-down menus. In dependence of the methodology used, the user is guided through different field sets.

In the subsequent discussion, the issue has been addressed when an enzyme converts one substrate to multiple products (e.g. hydroxylation at different positions). Neither for this case nor for non-Michaelis-Menten kinetics parameters a solution could be provided even though both cases are considered essential.

ACTION POINTS

- Carsten: draft of standards for reporting enzyme mechanisms
- Carsten: suggestion on the inclusion into the STRENDA guidelines (if possible)

EnzymeML - Status, progresses and perspectives

(presented by J. Pleiss)

Philosophy of EnzymeML:

- an extensible data model,
- currently, adaptable and scalable workflows which implement best practices on data reporting and modelling and figure out ways to analyse HT experimental data,
- structured data for mechanistic and data-driven modelling suitable for the development of additional tools and repositories and to contribute to the extension of existing ELNs.



News

- extension of the group of EnzymeML partners in order to create and test use cases for the extension of EnzymeML,
- test of data transfer from the "bench" to modelling platforms,
- connection with electronic lab notebooks developers in order to incorporate EnzymeML,
- development and test of data transfers into databases and repositories,
- EnzymeML webinar series with monthly talks and subsequent discussions
- · many posters and talks presented,
- 4th EnzymeML Workshop about to take place end of September with about 30 participants

(see the program here:

https://www.beilstein-institut.de/en/projects/strenda/meetings/4th-enzymemlworkshop/).

Extending the STRENDA Guidelines - Reporting Guidelines for Biocatalysis Experiments

(short presentation by Carsten and Jürgen)

The working group with S. Malzacher, D. Rother, Z. Findrik-Blažević, R. Giessmann, P. Halling, C. Kettner, J. Pleiss, J. Range, K. Rosenthal, P. Wied, R. Wohlgemuth, and J. Woodly is currently working on the extension of the STRENDA Guidelines towards the inclusion of reporting of data from biocatalysis experiments (as proposed in the paper by Gardossi et al. (2010), DOI:10.1016/j.tibtech.2010.01.001).

In contrast to the procedure when the STRENDA Guidelines were created, this extension is generated in a modularized way:

- use cases were determined by the experts in the field for the description of the modules,
- the modularization was directly implemented in a software-based decision tree (see https://github.com/StephanM87/Strenda-biocatalysis),
- an experimental workflow with regards to the data reporting was generated,



• meta-data are defined in parallel to the definition and description of the experimental procedures,

The STRENDA Biocatalysis Reporting Guidelines have reached their version 1.0 and will be published in the very near future (manuscript is circulating within the working group).

Recommendations for kinetic modelling

(Santiago Schnell)

No further progress due to a high work load by Santiago. He will report at the next meeting.

Proposal: Standard Conditions and Standard States for physiological Chemistry

(presented by H. Westerhoff)

Decision made in 2020 to draft a paper that presents the description of the underpinning thermodynamics in addition to the Recommendations paper published by Goldberg et al. In BJOC (https://doi.org/10.3762/bjoc.19.26). At the last meeting, Hans was assigned to work on the complete thermodynamic basis and in his presentation he discussed how to deal with activity coefficients, why should one use a pH buffer, how to deal with hydration and which standard conditions should be chosen and why. In particular, he focused on the recommendation of standard conditions of for physiological chemistry rather than applying those defined for physical chemistry. In summary, he proposed the following

p = 1 bar (= 10^5 N/m²), T = 310 K (37° C), standard concentration = 1 mM (and 1 mbar for gases), ionic strength = 0.15 M.

A proposed standard medium would look like this:

- Phosphate:
 - ∘ pKa phosphate =6.7
 - o 3.33 mM K₂HPO₄
 - 1.67 mM KH₂PO₄
- 1 mM MgCl₂
- 1 mM CaCl₂



- 10 mM Na_{glutamate}
- 132.3 mM K_{glutamate}
- pH=7.0, pMg=3, pCa=3, [K⁺] =140 mM, [Na⁺] = 10 mM, [Pi] = 5 mM, 142 mM [Glutamate= = 142 mM
- (Mg and phosphate hardly bind under these conditions [Alberty 2006 page 19])
- If there are Mg binders amongst the metabolites, add the latter (effectively) as the K_{salts} , compensate with the amount of $K_{\text{glutamate}}$ and increase the amount of MgCl₂ with the amount of that metabolite.

This proposal has been extensively discussed regarding

- the applicability of the standard states,
- the recommendations of standard conditions for both enzyme kinetics and modelling
- the role of the STRENDA Commission being the "authority" to propose these standards
- · how to proceed.

The Commission agreed that these proposed standard states for physiological chemistry are feasible and more over, they should be recommended for both enzyme kinetics and modelling.

There was a serious discussion whether STRENDA would be the appropriate body to propose these "new" standards. The general perspective was that as there has not been and there is no other body willing to spend efforts into making considerations and proposals towards the definition of less error-prone and more "user" friendly thermodynamic standard states, there should be no objections to STRENDA taking on the task. Of course, it would be essential to invite scientists from IUPAC and IUBMB and others who are known to be experienced in the application of thermodynamics principles. The purpose(s) is to receive more feedback and to increase the acceptance of these recommendations by the wider community.

The Commission agreed with HW that this underpinning paper would be a useful addition to the Recommendations paper and encouraged HW to proceed. However, the decision has made to draft two papers: a short version that briefly introduce into the recommendations of the standard states for physiological chemistry. The second draft will be the long version which has been already circulating within the Commission and which explains in detail the theoretical basis for the new conditions.



ACTION POINTS

- Hans prepares a short version of the paper, and this manuscript will circulate within the Commission seeking for feedback,
- Hans contacts scientists outside of STRENDA, in particular from IUPAC and IUBMB and others,
- the long version will be converted into a GitHub or LaTex version which makes it easier to track changes (Johann, Athel).

openTERC – open database on thermodynamics of enzyme catalyzed reactions

(Robert Giessmann)

Robert presented openTERC, an open database on thermodynamics of enzyme-catalyzed reactions which closely cooperates with eOuilibrator the project (https://equilibrator.weizmann.ac.il/static/classic_rxns/index.html) that calculates the formation of Gibbs Energy as a function of pH and ionic strength. He has established a network of about 30 scientists interested in thermodynamics of biochemical reactions that contribute. His main platform is GitHub (unfortunately, no URL available).

General

EC numbers no longer required by journals?

Obviously, EC numbers are rarely included in publications. Andrew is maintaining the EC system and currently adds roughly 30 new EC entries per year.

ACTION POINTS

Carsten:

- draw a landscape of the STRENDA project
 (see e.g. for MIRAGE: http://tinyurl.com/38dt4j4z)
- making the STRENDA inspired and related projects visible