

AGREEMENT

BETWEEN

Forschungszentrum Jülich GmbH

52425 Jülich

Federal Republic of GERMANY

- hereinafter referred to as “Forschungszentrum Jülich” or “PUBLISHER”

AND

Institute

Department

Street Address

City

State/ Province

ZIP/ Postal Code

Country

represented by

Family name

First name

Email

- hereinafter referred to as “LICENSEE”

- hereinafter also referred to as “PARTY” and/ or “PARTIES”

CONCERNING

Use of the Software Suite **13CFLUX2**

Please read through carefully

PRAEAMBLE:

Within the Modeling and Simulation Group of the IBG-1: Biotechnology, affiliated to the Forschungszentrum Jülich GmbH, the author Michael Weitzel and co-authors have developed the software suite **13CFLUX2**. Forschungszentrum Jülich holds all intellectual rights, titles and interests in **13CFLUX2** and is interested to have other research groups and educational institutes to also use the software.

The LICENSEE is strongly interested in obtaining a license for using the **13CFLUX2** software from Forschungszentrum Jülich for **non-commercial and/ or educational purposes**. On the assumption of a non-commercial use of **13CFLUX2** Forschungszentrum Jülich is pleased to give you the right to use the software submitting the following conditions:

1. Description of the Software

The "PUBLISHER" has designed and developed **13CFLUX2** which consists of a set of applications for performing ^{13}C -based Metabolic Flux Analysis (^{13}C -MFA), i.e. the simulation-based estimation of *in-vivo* metabolic reaction rates. In particular, the implemented type of ^{13}C -MFA relies on ^{13}C labeling measurement data obtained from an organism which is kept under metabolic and isotopic stationary conditions. The ^{13}C labeling measurement data are usually (but not necessarily) generated using mass spectrometry (MS) or nuclear magnetic resonance (NMR) measurement devices.

The estimation of *in-vivo* reaction rates for very large metabolic networks, the evaluation of a series of high throughput experiments, as well as the evaluation of nonlinear statistics and experimental design involves a high computational effort. By implementing newly developed simulation algorithms, which are highly tuned for the underlying mathematical problems, using **13CFLUX2** allows to perform ^{13}C -MFA studies on a common desktop computer. Network models and measurements are authored in the FluxML document format.

Unique characteristics of the **13CFLUX2** software suite are:

- significantly improved performance and higher numerical accuracy compared to the predecessor version 13CFLUX and other available software packages for ^{13}C -MFA;
- professional input and output via XML-based file formats and HDF5 (hierarchical data format, version 5);
- a comprehensive error handling including comprehensible error messages;
- statistical analysis of the obtained reaction rate distribution and tools for performing optimal experimental design;
- support for multi-core CPUs and computer clusters.

The following license terms apply to the software's executable files as well as to the included manuals and data files (in this agreement referred to as the "SOFTWARE"). Likewise, these terms apply to any **13CFLUX2** software update provided by Forschungszentrum Jülich GmbH, unless separate license terms accompany those items. If so, those license terms apply.

BY INSTALLING AND/ OR USING THE SOFTWARE, YOU ACCEPT THE TERMS OF THIS LICENSE AGREEMENT. IF YOU DO NOT ACCEPT IT, DO NOT INSTALL AND USE THE SOFTWARE. IF YOU COMPLY WITH THESE LICENSE TERMS, YOU HAVE THE RIGHTS AS SPECIFIED BELOW.

2. Conditions

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2.5. For the avoidance of doubts, no commercial use of SOFTWARE is allowed without the prior written consent of PUBLISHER.

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2.7. In the case of publishing or dissemination as well as oral presentation of results which refer to SOFTWARE or which contain results obtained by the use of SOFTWARE, PUBLISHER has to be mentioned as the owner and developer of the SOFTWARE by citing

Weitzel, M., Nöh, K., Dalman, T., Niedenführ, S., Stute, B., Wiechert, W.
13CFLUX2 - High-Performance Software Suite for 13C-Metabolic Flux Analysis
Bioinformatics 2012; doi: 10.1093/bioinformatics/bts646

as well as mentioning the internet site <http://www.13cflux.net>.

2.8. LICENSEE shall inform PUBLISHER in writing about any errors and deficiencies detected.

2.9. For the avoidance of doubts, any use exceeding the above mentioned scope, in particular, but not limited to, within the framework of commercial services rendered to or cooperation entered into with third parties, are subject to a separate agreement.

3. Costs

SOFTWARE is provided free of charge. Cost for shipping, handling and installation (e.g. travel) if applicable, are borne by LICENSEE.

4. Documents and Submission of Documents

4.1. The intellectual rights on documents created by LICENSEE using SOFTWARE, source code and the derived binary forms if software extensions developed by LICENSEE by using the development environment of SOFTWARE remain with LICENSEE.

4.2. IN ORDER TO ENSURE AN EXCLUSIVE NON-COMMERCIAL USE OF "SOFTWARE", IT IS NECESSARY TO SUBMIT RELATED INPUT DOCUMENTS (CONTAINING METABOLIC NETWORK SPECIFICATIONS AND MEASUREMENT DATA) TO "PUBLISHER" FOR THE PURPOSE OF STORING AND MAYBE INSPECTING THE CONTENTS. IN THIS CASE "PUBLISHER" HAS NO RIGHT TO USE THE CONTENTS OF THE SUBMITTED DOCUMENTS (AS WHOLE OR IN PART) FOR PUBLICATION OR ANY COMMERCIAL OR OTHER PURPOSE, EXCEPT AS EXPLICITLY STATED IN THIS ARTICLE 4.2. FURTHERMORE, "PUBLISHER" SHALL ENSURE THAT ALL SUBMITTED DOCUMENTS ARE TREATED CONFIDENTIALLY. IN PARTICULAR, THIS MEANS THAT "PUBLISHER" HAS TO TAKE CARE THAT SUBMITTED DOCUMENTS ARE FILED IN A NON-PUBLIC AND TECHNICALLY SECURED LOCATION WHICH MAY ONLY BE INSPECTED BY TWO SELECTED EMPLOYEES OF "PUBLISHER".

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LICENSEE is not entitled to alter or reverse engineer SOFTWARE in any way. The right to alteration of the SOFTWARE remains with PUBLISHER.

6. Alterations of this License Agreement

Any modifications and amendments to this agreement shall be made in writing. Should any provision of this agreement be ineffective or void, this shall not affect the validity of the other contractual provisions. Such invalid provision should rather be replaced by a valid provision as close as possible to the invalid provision.

7. Transferability of Rights and Obligations

Rights and obligations arising out of this agreement can be transferred to third parties only after written consent by the other party.

8. Terms of Agreement

This agreement shall come into force upon execution by both parties until 31st December 2021. Thereafter it shall automatically renew for another two years if not terminated by at least one of the parties with six month notice. Termination notice must be given in writing or by using the electronically provided procedure for termination. In case of misconduct and/ or failure to comply with any terms of this agreement PUBLISHER can immediately terminate the agreement without further notice. In the event of termination of this agreement LICENSEE is obliged to remove the programs from all data processing systems installed. If not agreed otherwise between the parties, LICENSEE shall comply with this obligation by deleting SOFTWARE from all data storage media.

9. Jurisdiction

This agreement shall be governed by the law of the Federal Republic of Germany. The Parties will settle all differences in connection with this agreement including its legal validity and effectiveness after termination on a partnership basis. If any disputes in connection with this agreement or its validity cannot be settled on a partnership basis, they shall be finally settled pursuant to the rules of the German Arbitration Institution (DIS -Deutsche Institution für Schiedsgerichtsbarkeit e.V.) by a court of arbitration, any recourse to courts of law being excluded. The place of the arbitration proceedings shall be Jülich. The language of the arbitration proceedings shall be German. The jurisdictions of the courts of law shall not be affected for measures of temporary relief. The place of jurisdiction shall be the administrative headquarters of PUBLISHER.

Forschungszentrum Jülich GmbH

Jülich, Germany,

Dr. C. Cremer

Head Innovation and Strategy
Corporate Development

Prof. Dr. W. Wiechert

IBG-1: Biotechnology

Forschungszentrum Jülich