People's Democratic Republic of Algeria

Ministry of Higher Education and Scientific Research

Mohamed Sedik Ben Yahia University – Jijel

Faculty of Natural and Life Sciences

Department of Molecular and Cellular Biology

MASTER I Applied Biochemistry

Module: Free and Open-Source Software

Practical Work Report

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PART 1 – Theoretical Study of a Tool: COPASI

I- Introduction:

COPASI which stands for COmplex PAthway Simulator, is an open-source software application for creating and solving mathematical models of biological processes such as metabolic networks, cell-signaling pathways, regulatory networks, infectious diseases, and many others. It is built upon the legacy of the GEPASI simulator software that was developed in the early 1990s by Pedro Mendes. The initial development of COPASI was funded by the Virginia Bioinformatics Institute, and the Klaus Tschira Foundation. Current development efforts are supported by grants from the National Institute of Health, the BBSRC, and the German Ministry of Education.

COPASI is the result of an international collaboration between the University of Manchester (UK), the University of Heidelberg (Germany), and the Virginia Bioinformatics Institute (USA). The project principal investigators are Pedro Mendes and Ursula Kummer. The chief software architects are Stefan Hoops and Sven Sahle.[1]

To ensure broad accessibility within the scientific community, Source and binary distributions are available from the COPASI Website (http://copasi.org) for Windows, Linux, and Mac OS X. This makes it very easy for researchers to install COPASI and get started quickly.[2]

II- Features:

1- Model Construction and Standards:

- [3]Model Editing: Models are entered in (bio)chemical terms. (Bio)chemical species, located in compartments, can be transformed through reactions. The rate of each reaction is given by a kinetic rate law, that can be either selected from an included function database (filtered to apply to the selected reaction), or freely defined. Additionally, discrete events can be added to the model, that change model elements based on arbitrary expressions. From this formalism, COPASI derives the mathematical representation of the model automatically.

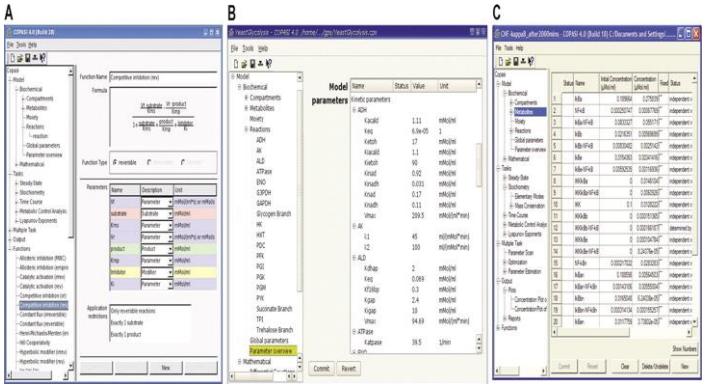

Figure 1 COPASI's interface for model editing

- Model Standards: COPASI stores the model and information what to do with it in its own specialized XML format. However, wherever possible, applicable community standards are supported. Models can be imported and exported in the Systems Biology Markup Language format, where all major versions are supported.

2- [4]Simulation and Dynamical Analysis:

- Simulation Algorithms: At the core, COPASI supports two main formalisms for simulating the dynamics of the defined model (time course simulations). One is the traditional chemical kinetics approach of using ordinary differential equations (ODE), where the software uses the LSODAR integrator. The second is the stochastic formalism, where individual reaction events are drawn from probability distributions, using either of the following algorithms: Gillespie's Direct Method, Gibson-Bruck, τ-Leap, or adaptive SSA/τ-leap.

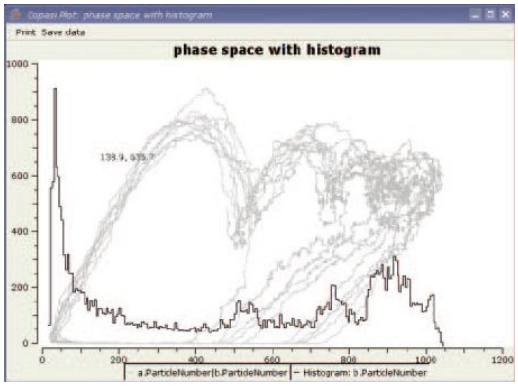

Figure 2 Figure showing Stochastic vs. Deterministic Oscillations

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[1] de.NBI. (n.d.). Introduction to COPASI. https://www.denbi.de/online-training-media-library/395-introduction-to-copasi

[2] Bergmann, F. T., Hoops, S., Klahn, B., Kummer, U., Mendes, P., Pahle, J., & Sahle, S. (2017). COPASI and its Applications in Biotechnology. Journal of Biotechnology, 261, 215. https://doi.org/10.1016/j.jbiotec.2017.06.1200

[3] Hoops, S., et al. (2006). COPASI—a COmplex PAthway SImulator. Bioinformatics

[4] Bergmann, F. T., et al. (2017). COPASI and its applications in biotechnology. Journal of Biotechnology.

[5]3. Analysis and Optimization Tasks:

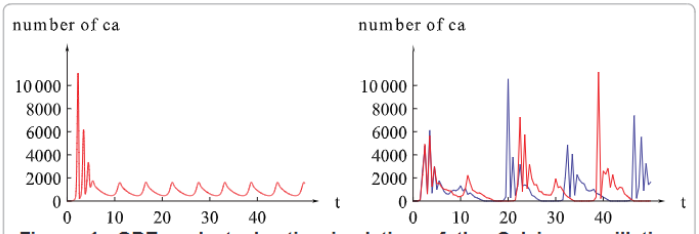

Figure 1: ODE and stochastic simulation of the Calcium oscillation model. The graphics on the left side shows an ODE simulation of the Calcium oscillation model. The graphics on the right side shows two stochastic realizations of the Calcium oscillation system. Parameters and initial values as given in the results section.

- Analysis Tasks: The model evaluations through time course simulations or steady state computations at the core of COPASI support a number of additional analysis tasks.
    - Parameter Scan: The parameter scan task can be used to run any of the other tasks repeatedly.
    - Optimization: In the optimization task users can enter an arbitrary expression of model quantities (or even results from the execution of other tasks) that should be maximized or minimized.
    - Parameter Estimation: Parameter estimation is the activity of changing the model's parameter values in order to make the behavior of the model as close as possible to a set of experimental measurements.
- Metabolic Control Analysis: Metabolic control analysis (MCA) is a special type of sensitivity analysis that calculates how much a perturbation in the rate of a reaction affects the steady state concentrations or fluxes.
- Sensitivities: Sensitivities provide a measure of how much a selected model variable (the effect) changes when a selected parameter (the cause) is changed.

III- Technical aspects:

The technical robustness of COPASI is constructed upon high-overall performance numerical libraries and a modular structure that separates the person interface from the computational core.

1. Core Mathematical Engines Deterministic Integration: COPASI makes use of **LSODAR** (Livermore Solver for Ordinary Differential Equations), an advanced set of rules that routinely detects "stiffness" in a system. This lets in the software program to exchange among one of a kind numerical method (Adams and BDF) to keep balance even if response speeds range with the aid of using numerous orders of magnitude.
    - Stochastic Precision: For structures in which randomness is critical, it implements the **Gibson-Bruck** model of the Next Reaction Method. This is a computationally green variation of the Gillespie set of rules that makes use of a **dependency graph** to best replace affected reactions, notably lowering CPU time.[6]
    - Hybrid Solvers: To stability velocity and accuracy, COPASI capabilities **Hybrid (Runge-Kutta)** and **Hybrid (LSODA)** solvers. These dynamically partition the model, treating species with low particle numbers stochastically at the same time as the use of differential equations for extra considerable species.[7]
2. Software Engineering and Standards Development Language: Written in **C++**, the software program guarantees high-velocity execution for CPU-extensive responsibilities like international optimization and large-scale parameter scans.
    - Interoperability: It is constructed on **libSBML**, supplying complete aid for the **Systems Biology Markup Language (SBML Levels 1-3)**. It additionally helps **SED-ML** (Simulation Experiment Description) and **COMBINE archives**, which standardize how simulation "experiments" (now no longer simply models) are shared.
    - Programmability: Beyond the GUI, COPASI is offered thru **C++, Python (basiCO), and R (CoRC).** This lets in researchers to automate workflows and combine COPASI`s math engine into large bioinformatic pipelines.[8]

IV- Strengths & Limitations and weaknesses:

The following table is resuming strengths points and limitations, weakness of the COPASI tool.

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[5] *Zimmer, C., & Sahle, S. (2012). Parameter estimation for stochastic models of biochemical reactions.*

[6] *Bergmann, F. T. (2023).* "BASICO: A simplified Python interface to COPASI." *Journal of Open Source Software*, 8(90), 5553.

[7] *Bergmann, F. T., et al. (2017).* "COPASI and its applications in biotechnology." *Journal of Biotechnology*, 261, 215–220.

[8] *Bergmann, F. T. (2023).* "BASICO: A simplified Python interface to COPASI." *Journal of Open Source Software*, 8(90), 5553.

Category	Strengths (Advantages)	Limitations & Weaknesses
Usability	No programming required: Graphical interfaces allow biologists to build complex models without writing code.	Steep Learning Curve: The huge number of menus and advanced mathematical settings can be overwhelming for beginners.
Performance	High-speed C++ Core: Very effective for solving large ODE systems and iterative optimization problems	Memory Intensity: Large stochastic simulations and large parameter scans can be very memory intensive.
Features	All-in-one Toolkit: combines modeling, parameter estimation, and MCA in one package.	Visualization Limits: While functional, the inherent plotting tools are deficient in variety compared to modern libraries like Matplotlib or ggplot2.
Integration	Standard Compliance: Better SBML support allows models to work with a variety of software.	Scripting Complexity: While APIs such as BASICO and CoRC are accessible, they require separate installation and a basic comprehension of Python or R.
Mathematics	Robust Solvers: Uses LSODA for "hard" systems, providing numerical stability even when other tools fail.	Local Minima: As with any optimization tools, selecting an inappropriate algorithm may result in the user becoming ensnared in a local minimum.

Table 1 Strength VS limitation and weaknesses of COPASI

V- CONCLUSION:

In summary, COPASI has established itself as an essential foundation for computational systems biology. By combining intuitive biochemical modeling with advanced numerical analysis, researchers can move from static descriptions of developmental pathways to a dynamic and predictive understanding of life. Its great strength comes from its flexibility, which allows for a smooth switch between deterministic and stochastic formalisms, and its strength, which is shown by its strict adherence to worldwide community standards like SBML and SED-ML.

Since 2026, the program has continued to evolve, as indicated by the release of COPASI 4.46 in January. With the advent of innovative tools like **sbmodelr** for large-mesh modeling and expanded support for hybrid modeling (combining mechanical models with machine learning), COPASI is a leader in this sector[9]. For both academic research and industrial biotechnology, COPASI offers the high-performance engine required to turn experimental data into valuable biological information, assuring its continuous utility in an increasingly data-driven scientific world.[10]

[9] COPASI Team. (2026). Release Notes for COPASI 4.46 (Build 300). https://copasi.org/News/2026/01/23/Release/..

[10] Smith, L. P., et al. (2025). Verification and reproducible curation of the BioModels repository. PLOS Computational Biology.

PART 2 – Practical Study: Exploration of Zenodo:

I. Presentation of Zenodo:

Zenodo, named after Zenodotus, was created by CERN as an open-source and free repository for storing data, code, materials and any research artefact. Zenodo was launched on May 8, 2013, as the successor of the OpenAIRE Orphan Records Repository to allow researchers in any subject area to comply with any open science deposit requirement absent an institutional repository.

Zenodo is a multi-disciplinary open research repository hosted by CERN and commissioned by the European Commission through the OpenAIRE project to support the Open Data and Open Access movements in Europe. Data, software and all research-related digital artefacts up to 50 GB in all formats and from any stage of the research lifecycle can be submitted. All uploads are assigned with a digital object identifier (DOI) to make them citeable.[11]

1. Platform objectives:

- Digital Object Identifier (DOI)
- Open Access Research Repository
- FAIR Principles
- Open Licensing
- Metadata and Searchability
- Secure and Long-Term Preservation
- Analytics and Impact Measurement[12]

2. Types of hosted content:

Zenodo accepts almost any digital artifact related to research:

- All fields of research.
- All types of research artifacts (Includes journal articles, preprints, conference papers, books, reports, and theses).
- All formats are allowed, with a size limit of up to 50 GB per record.
- All metadata is stored internally in JSON-format according to a defined JSON schema. Metadata is exported in several standard formats such as MARCXML, Dublin Core, and DataCite Metadata Schema (according to the OpenAIRE Guidelines).[13]

3. Importance of Zenodo for open science and research in NLS:

Zenodo offers researchers a user-friendly, reliable, and scalable platform for sharing and preserving virtually unlimited amounts of research outputs. Its commitment to open access, long-term preservation, version control, and integration with other platforms make it a valuable tool in the research community.[14]

II. Description of the steps carried out:

1. Search performed & Dataset selection criteria:

The query used to search is "**Tissue regeneration**", I chose the topic of **Neurogenesis in status epilepticus** because it represents an important today topic in neuroscience, the balance between pathological brain rewiring and compensatory repair. This subject allows for the exploration of diverse biological data, from tissue-level histological changes to molecular-level gene expression, all of which are well-represented on the Zenodo platform with an easy organized form.

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[11] Gurav, V., & Nagarkar, S. R. (2025). ZENODO: A PLATFORM FOR OPEN ACCESS AND SUSTAINABLE DIGITAL RESEARCH REPOSITORY. TechnoLibrarianship: A Gateway Towards Future Libraries-2025, Shivaji University, Kolhapur, PP-152-159.

[12] Gurav, V., & Nagarkar, S. R. (2025). ZENODO.

[13] https://about.zenodo.org/policies/

[14] Crespo Garrido, I. D. R., Gutleber, J., & Loureiro García, M. (2025). Springer: The Value of an Open Scientific Data and Documentation Platform in a Global Project: The Case of Zenodo.

2. Platform navigation:

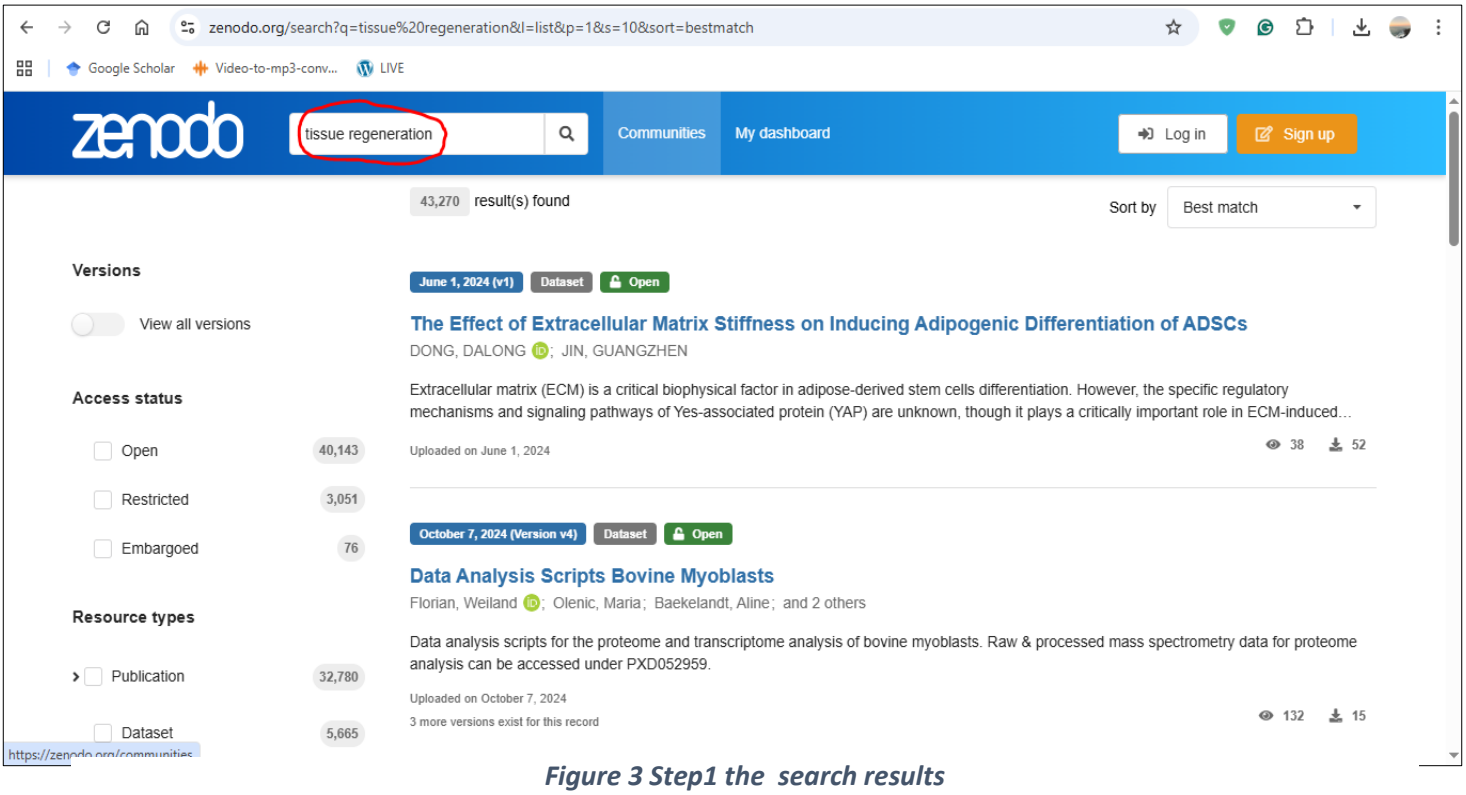

Figure 3 Step1 the search results

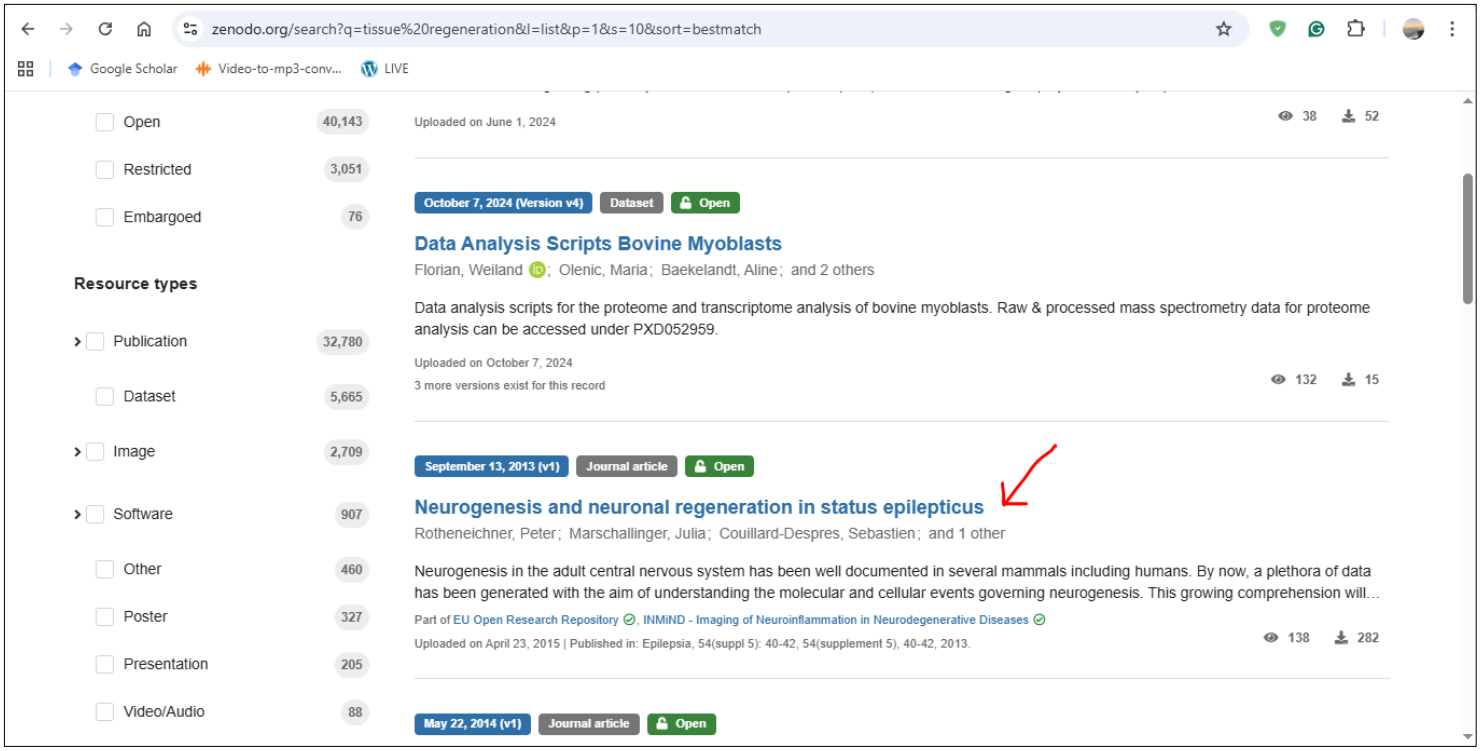

Figure 4 Step 2 Selected data

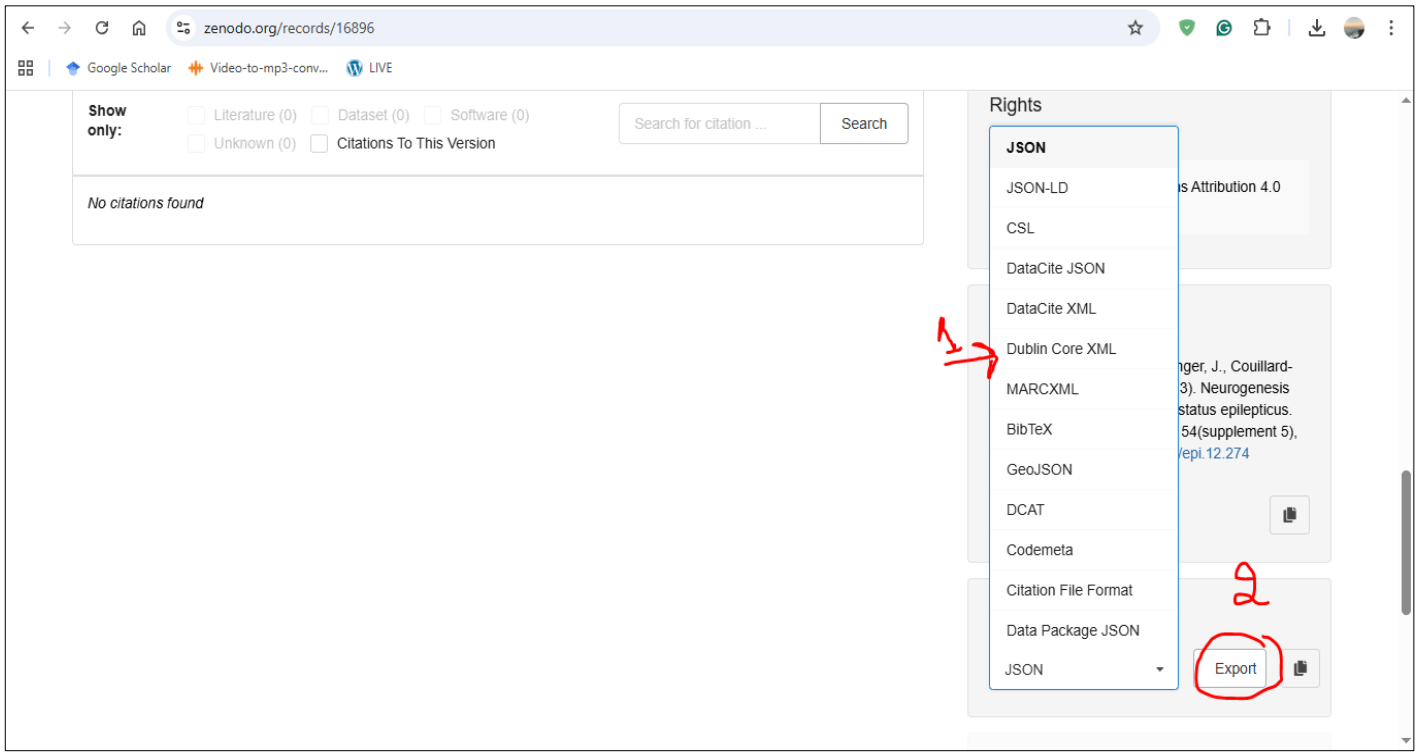

Figure 5 Step3 Download action

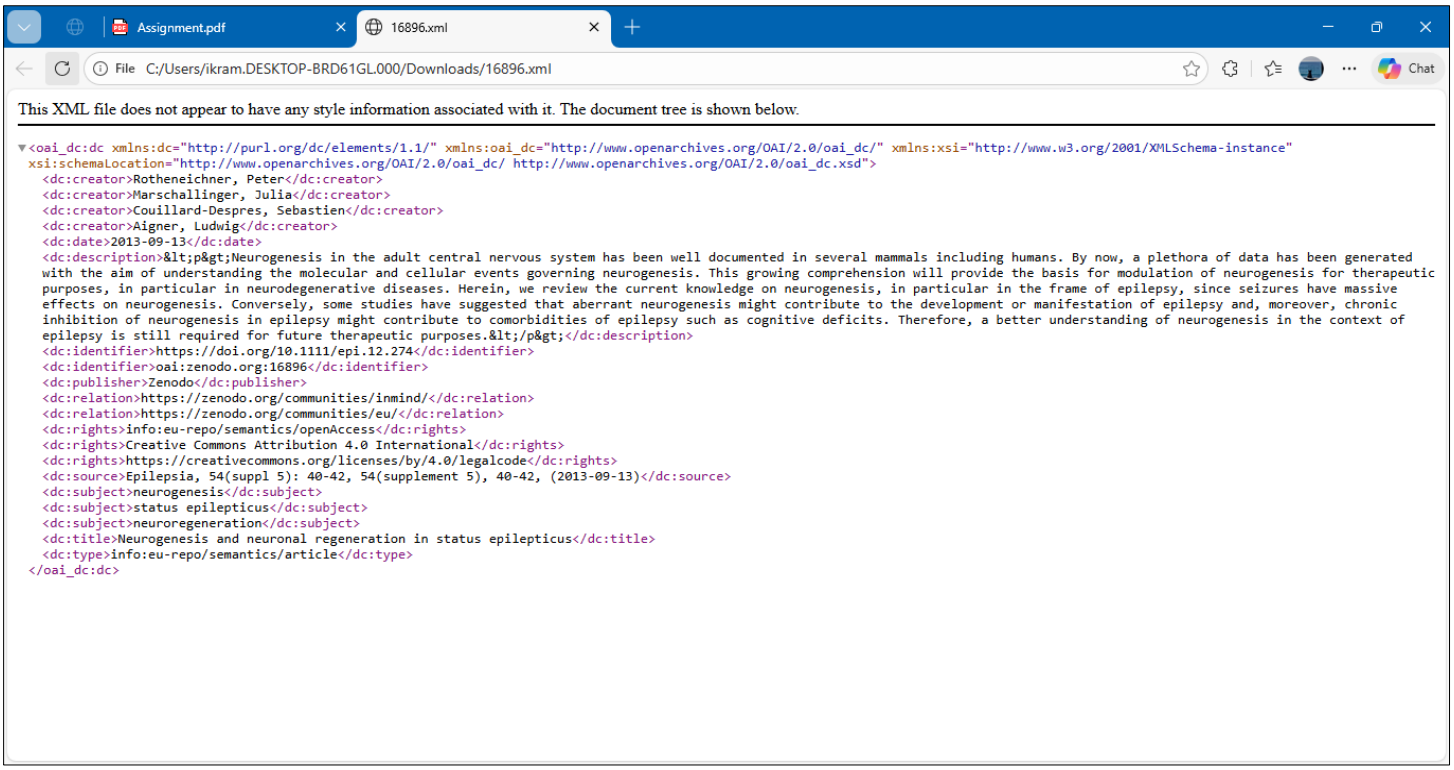

Figure 6 The dataset

III. Dataset metadata:

Element	Definition
Creator	Rotheneichner, Peter; Marschallinger, Julia; Couillard-Despres, Sebastien; Aigner, Ludwig
Date	2013-09-13
Description	Neurogenesis in the adult central nervous system has been well documented in several mammals including humans. By now, a plethora of data has been generated with the aim of understanding the molecular and cellular events governing neurogenesis. This growing comprehension will provide the basis for modulation of neurogenesis for therapeutic purposes, in particular in neurodegenerative diseases. Herein, we review the current knowledge on neurogenesis, in particular in the frame of epilepsy, since seizures have massive effects on neurogenesis. Conversely, some studies have suggested that aberrant neurogenesis might contribute to the development or manifestation of epilepsy and, moreover, chronic inhibition of neurogenesis in epilepsy might contribute to comorbidities of epilepsy such as cognitive deficits. Therefore, a better understanding of neurogenesis in the context of epilepsy is still required for future therapeutic purposes.
Identifier	**DOI :** https://doi.org/10.1111/epi.12274
	OAI: zenodo.org:16896
Publisher	Zenodo
Relation	Zenodo Communities: inmind, eu
Rights	Creative Commons Attribution 4.0 International; Open Access https://creativecommons.org/licenses/by/4.0/legalcode
Source	Epilepsia, 54(suppl. 5) : 40-42, (2013-09-13)
Subject	Neurogenesis ; status epilepticus ; neuroregeneration
Title	Neurogenesis and neuronal regeneration in status epilepticus
Type	info:eu-repo/semantics/article

Table 2 DATASET METADATA

The metadata above was extracted using the Dublin Core format from Zenodo.