

# An update of the Bachmann COMBINE archive

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## Abstract

**Introduction:** The increase of size and complexity of simulation studies in systems biology and systems medicine proposes new challenges to sharing reproducible results. The Computational Modeling in Biology Network (COMBINE) improves the coordination of standard formats for several features of simulation studies [11]. On the other side, GitHub has been used as an essential common platform for managing software projects and supporting collaborative development [4].

**Methods:**

**Results:**

**Conclusions:**

**Keywords:** Systems Biology, Computational Biology, Data Science, Medical Informatics, COMBINE, containers, data

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# Introduction

## Scientific background

The increase of size and complexity of simulation studies in systems biology and systems medicine proposes new challenges to sharing reproducible results. The Computational Modeling in Biology Network (COMBINE) improves the coordination of standard formats for several features of simulation studies, such as Systems Biology Markup Language (SBML), CellML, Systems Biology Graphical Notation (SBGN), Systems Biology Graphical Notation (SBGN), and Systems Biology Result Markup Language (SBRML). These standards aim to encode, simulate and visualize biological models [11].

On the other side, GitHub has been used as an essential common platform for managing software projects and supporting collaborative development. Now a day some educational projects have begun to adopt it for hosting and managing course content because it gets transparency features to create, reuse, and remix materials; and to monitor activity on assignments and projects [4].

## Rationale

## Objectives

## Materials and methods

The purpose of this project was divided into four groups. The tasks of each of them were the management of a documentation platform, review of exiting materials, comparison of provided models, graphical representation, and supply of a model script.

To provide the model from Bachmann *et. al.*[1] as a Fully Featured COMBINE Archive, we have created a public repository using the open-source platform GitHub, with a CC0-1.0 License. We choose GitHub as a data management platform to supervise the course of the project because it provides an intuitive and easy customizable environment, along with some features for documentation, and agile project management [4]. This repository contains the proposal directory's structure from Scharm & Waltemath [11] with the directories documentation, model, experiment, and result.

To achieve this goal, we research the literature about the Bachmann model and the COMBINE Archive, along with modeling file formats, checking the reproducibility of the COMBINE structure and software tools that had been used. In addition, we established communication channels, developed a rough schedule, provided a template for documentation, and periodically reviewed intermediate deliverables.

In our research, we found six SBML-Bachmann models in two different repositories, JWS Online and BioModels (see Results). We choose the last model from 14th November 2019 to perform other tasks in our project, because it provides complementary files for the simulation.

We found and tested five software tools for the simulation of biological systems. JWS Online, Systems Biology tool for the construction, modification, and simulation of kinetic models and the storage of curated models [7]; on this repository was one of the found models. Webviewer Uni Rostock (CombineArchiveWeb), a tool to visualize and manage COMBINE files [11]; this is the goal application of our project. COPASI, a software application for the simulation and analysis of biochemical networks and their dynamics

[9]. SED-ML, a suite of tools for creating, editing, simulating and validating SED-ML files [13]. Tellurium, a tool to model, simulate and analyze biochemical systems [5].

One of the objectives of our project was to provide a standardized graphical representation of the Bachmann model based on the SBGN. Consequently, we performed research but we do not found any SBGN of this model. Therefore, we decided to create an SBGN network *de novo* based on Le Novère [6] and Touré *et. al.* [12]. In this step, we select the SBGN language, and lastly, we created the Process Description (PD) map with the web tool Newt Editor (v3.0.3) [2]. To validate the SBGN-ML we imported it into several software and libraries, LibSBGN from Newt Editor, the open-source software Visualisation and Analysis of Networks containing Experimental Data (VANTED) [8], Krayon for SBGN [3], and SBGNViz [10]. Lastly, we cleaned up the map and colored the relevant features in the model to improve the developed map.

We created new SED-ML files to reproduce some experiments from Bachmann *et. al.* in combination with another model. Following research for tools for building SED-ML files, we determined to divide our approach into, default simulations using the WebTool COPASI, and experiment-specific simulations using Tellurium. After the validation, the new SED-ML, and the supplementary output files were inserted into the COMBINE archive.

## Results

In our research, we found six SBML-Bachmann models, one of them as support information of Bachmann *et. al.* [1], this was the first delivered model. The others come from two different repositories, JWS Online and BioModels.

We found three models on the repository of BioModels. The first, BIOMD0000000347\_url.xml, was submitted on 22nd July 2011 and modified on 31st January 2012. Together with this model were other files in different formats. Most of them were generated by tools to simulate, visualize, validate and document the model, one of them is another SBML model, BIOMD0000000347\_urn.xml. The third and newest, Bachmann2011.xml, was posted on 14th November 2019. This one has other complementary files for the simulation of this model. The models in JWS Online do not have any date of building or update, so we do not know when these were built. The first model in JWS online, bachmann.xml, is from *Mus musculus* and represents the STAT's pathway in a cell simulation *in silico*. The second model, bachmann2.xml, was obtained from the BioModels database (BioModels ID: BIOMD0000000347).

## Conclusions

**Authors' contribution:** The authors contributed equally to this work.

**Competing interests:** The authors declare no competing interests.

**Funding:** None.

**Acknowledgement:**...

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## Appendices

### GitHub Repository

Our public GitHub repository is available here: [https://github.com/ahodelin/Bachmann\\_Archive](https://github.com/ahodelin/Bachmann_Archive). This repository is a collaborative effort of participants of the module ”Bioinformatik und Systembiologie” in the Master Program BIDS, organized by the Graduate School Rhein-Neckar in cooperation with MIRACUM, a consortium of the Medical Informatics Initiative.

### COMBINE Archive

The fully featured COMBINE Archive of our project is available here: <https://cat.bio.informatik.uni-rostock.de/rest/share/6b507398-c103-4b92-9c90-d6b105ff1372> under the vignette **::bachmann**. The original publication with the used model (Bachmann *et. al.*) is available here: <https://doi.org/https://doi.org/10.1038/msb.2011.50>.