Towards Reproducible Digital Twins by Bridging COPASI with R

**Introduction**: Digital twins — i*n-silico* representations of biological systems — are generated by integrating empirical observations with established domain expertise. These *virtual Doppelganger* enable researchers to interrogate underlying biological processes and predict personalised responses to therapeutic interventions. Yet, despite a proliferation of computational tools, a persistent challenge lies in replicating the results of published studies, further exacerbating public scepticism towards scientific outputs [1], [2].

**Methods:** One promising avenue to address this reproducibility crisis is through collaborative, community-driven initiatives, with first and foremost coding events. Precisely, the purpose of the BioModels Hackathon, supported by Virtual Patient Engine and EMBL-EBI, was to curate a compendium of models up to the standards of BioModels. Specifically, the objective was to reproduce an ODE-based model of Inflammatory Bowel Disease originally presented in [3] within 48 hours with my team of 3 early-stage researchers. Subsequently, we curated the model to meet the rigorous standards of the BioModels repository and openly disseminating our results to the wider research community.

The process, however, revealed numerous roadblocks: datasets were only available as non-machine-readable PDF screenshots; no public GitHub/GitLab code repository existed for reproducing simulations, necessitating a complete reimplementation of the model’s equations; and the bespoke and unconventional nature of the modelling scenarios in [3] rendered standard point-and-click tools such as COPASI insufficient.

**Results**: To overcome these limitations, we extended COPASI’s capabilities using the R programming language, enabling:

* the implementation of advanced sensitivity analyses and statistical evaluations, not available in COPASI’s native interface,
* the integration of ggplot2 and Reactable for the automated generation of interactive, visual and tabular reporting of main paper’s insights.

**Code availability:** We deployed a reproducible Quarto website detailing our assumptions (when specificities of the methods were not properly reported within the paper), methodological adaptations, and results: <https://bastienchassagnol.github.io/COPASI_Team216_Lo2016/> .

**Conclusion**: This small project underscores the value of pairing open-source, scriptable frameworks with conventional modelling, point-and-click software, fostering reproducibility, and transparency.

[1] A. Desai, M. Abdelhamid, and N. R. Padalkar, ‘What is reproducibility in artificial intelligence and machine learning research?’, *AI Mag.*, vol. 46, no. 2, p. e70004, 2025, doi: 10.1002/aaai.70004.

[2] L. Udesky, ‘“Publish or perish” culture blamed for reproducibility crisis’, *Nature*, Jan. 2025, doi: 10.1038/d41586-024-04253-w.

[3] W.-C. Lo, V. Arsenescu, R. I. Arsenescu, and A. Friedman, ‘Inflammatory Bowel Disease: How Effective Is TNF-α Suppression?’, *PloS One*, vol. 11, no. 11, p. e0165782, 2016, doi: 10.1371/journal.pone.0165782.