BioModels Submission

* Names of the curators: 3 members of the team, Lilija, Sanjana, original authors of the paper? (which format, such as dc:creator) + Model Overview . 3 Levels: authors, submitter (me), and encoders.
* **It’s possible to update model after hand.**
* Main model (healthy conditions at steady state) + 4 sub-models corresponding to the 4 distinct endotypes and presenting distinct parametrisations -> automatically paired based on PubMed ID.
* What to submit?
  + SBML (which version? -> with COPASI, the latest is Level 3 Version 1) : + cps file (copasi). Use PubMed ID. Add in `Model/Details` abstract and curators (date) for the model + context (Hackathon event)
  + COMBINE archive format? (or simply redirect to GitHub Pages?) -> + file names only containing acceptable characters (alphanumeric characters, spaces, hyphens and underscores)
  + Datasets (IBD subgroups dgea and parametrisations)
  + Results (html, **csv** for Tables Results, or Excel concatenating everything?)? **Png** figures for figures.) R scripts? (around 10 files overall) -> GitHub Link.
  + Add renv to get a snapshot of the R packages used.
  + Do not forget to publish it afterwards.
* Model’s title: Lo2016 – IBD Response to Anti-TNFα treatment

## Additional resources:

* FAQ: <https://www.ebi.ac.uk/biomodels/faq>
* General guidelines for submission : <https://www.ebi.ac.uk/biomodels/model/submission-guidelines-and-agreement>
* Slides BioModels: <https://www.ebi.ac.uk/biomodels/user-guide/submission-guidelines/index.html#slide5>

A diagram of a workflow

AI-generated content may be incorrect.

‌‌Dear Professor Anais Baudot,

I'm writing to express my interest in your postdoctoral position titled "Hybrid AI for Organoid Digital Twinning.": <https://www.marseille-medical-genetics.org/en/a-baudot/postdoc-position-available/> I apologize in advance for the informal and rushed tone of this initial email—I’m reaching out on short notice but am genuinely enthusiastic about the opportunity.

I’m particularly drawn to the aspects of the project related to cell-cell communication inference and the development of in silico models that more closely reflect biological mechanisms, which strongly align with my current research interests and long-term goals.

## CCC Tools Inference Benchmark

I used to work for Professor AdLab’s laboratory, where my primary research focus was on developing a **robust benchmark for cell-cell communication (CCC)**algorithms. Precisely, acknowledging the vast number of CCC tools, we restrain its scope to comparing algorithms that simultaneously integrate **spatial transcriptomics (SRT)** with **intracellular signalling** captured by gene regulatory networks (GRNs). In addition, harnessing the *omnibenchmark* computational platform—a modular, community-driven and reproducible benchmarking computational framework with robust version control, developed by Professor Mark Robinson. One of the objectives was to minimise technical overhead (e.g., construction of Singularity images, CI/CD actions, parallelisation of processes) to focus instead on what matters, namely collecting relevant datasets, designing meaningful simulation frameworks (considering both a statistical point of view, using libraries such as *scMultiSim*, and mechanistic approaches, such as PhysiBoSS), and constructing biologically relevant metrics to assess GRN and ligand-receptor interactions reconstruction.

## CCC Tools Review and Methodological Innovations

Beyond benchmarking, I planned to:

1. Publish a review on CCC tools, starting from my continuously updated **notes** available here: [https://bastienchassagnol.github.io/CCCSTBench-Book/spatial-ccc-review.html](https://bastienchassagnol.github.io/CCCSTBench-Book/spatial-ccc-review.html#sec-CellPhoneDB) (I send you a private GitHub invitation link 😊). Beyond comparing existing approaches, the objective of this Quarto book is to identify methodological avenues of improvement of existing CCC tools for the third publication’s idea, choosing among one of the perspectives further highlighted.
2. Explore one (or several) of these improvement perspectives:
   1. From my **statistical**background, I believe we can refine existing permutation-based evaluations of ligand-receptor interactions' significance by leveraging variations of the **GEE regression or quantile-regression family** (both overlooking distributional assumptions about the residuals, while allowing, from their model-based philosophy, to include random effects and multi-samples and multi-batches conditions).
   2. Exploring how **CORNETO** could enhance CCC and signalling pathway predictions—building upon the Flow Network Optimization approach used in CellCom. Notably, CORNETO offers several advantages over CellCom, including an extension of the **CARNIVAL** toolkit for context-specific intracellular signalling inference, a **multi-sample framework** with additional regularization to penalise for network complexity, and **hypergraph**support that could be used to model signalling protein complexes (indeed, in most cases, all proteins belonging to a given signalling receptor must be activated simultaneously for a functional cellular communication event). The methodological innovation would consist of reframing CORNETO to handle a two-layer network structure—spanning across cell types (top level) and intra-cellular signalling (bottom level) (as done, in a deep learning framework, by CLARIFY: <https://academic.oup.com/view-large/figure/409581315/btad269f1.tif>‌)
   3. Enhancing deep learning approaches by refining generative modelling of dropout events. For example, instead of assuming negative binomial distributions (as in VAE-based DeepCOLOR), zero-inflated distributions—akin to those used in scPRINT—could better capture zero-inflated gene expression profiles. More broadly, I aim to integrate biological knowledge to refine the weighting of gene expression contributions.

## Additional Publications Projects

Finally, while not directly linked to the post-doc offer, I’m involved with:

* Michael Rera’s Drosophila aging team on developing the first deconvolution algorithm applied to bulk Drosophila samples for identifying biomarkers influential of the Smurf phenotype (on a side note, do you know the level of progress of the consortium paper on” Multimodal data integration to quantify tumour heterogeneity in cancer”?), including a trainee for running standard pre-processing analyses of single-cell RNASeq samples.
* Vera Pancaldi and Luca Grumulato on the first (up to my knowledge) cell line DNA Barcoding project with the objective of deriving drug fingerprints and predicting Mechanisms of Actions of unknown compounds, based on DNA Barcode counts.
* (Optionally, I would be pleased with getting statistical support to finalise my Ph.D. project on a network-based cellular deconvolution algorithm, DeCovarT, the first to my knowledge incorporating GRNs for enhanced delineation of closely related cell types).

Why I Am Reaching Out in such a panicked tone

I initially joined AdLab as a Professional Researcher but quickly requested a change in title to Postdoctoral Researcher, given the misalignment between my then official role and the broad scope of projects I was assigned to (Indeed, in addition to the five projects mentioned, my responsibilities included conducting a GWAS analysis, serving as the sole statistical expert in a team of 30 researchers, and developing a standardized Quarto-based Omics reporting framework—and I’m not even exhaustive!!) Unfortunately, it soon became clear that the postdoctoral position was largely symbolic, with no dedicated funding to support it. (The situation is actually even more complex than can be conveyed in the format of a mail; please feel free to reach out Vera for more detailed context.)

Without a rapid funding solution, I will likely be forced to abandon these promising projects, despite having initiated or co-initiated (as collaborations) most of them. I'm fully open to applying for external funding opportunities (such as EMBO or MSCA Postdoctoral Fellowships) and even exploring collaborations with external institutions (e.g., Institut Curie, Zürich’s lab, …). However, during the estimated 6–8 month waiting period for such grants, I cannot reasonably sustain myself on personal savings alone.

I’ll be returning to France this Friday and will give a 10-minute talk at the upcoming GT BioSS session next Monday, where I also plan to discuss potential funding options with Laurence Calzone (+ on a scientific side, exploring the development of more advanced simulation frameworks for the CCC benchmark with her PhD Victoria Bruning).

(On a side note, I already know and scientifically and humanly appreciate Florence Ghestem and Benjamin Loire through my involvement in the JeBiF association. I must admit initially reached out to Benjamin to get a quick feeling of the lab’s values—and I must say, they clearly better resonate with my own academic vision, emphasising strong, cross-disciplinary collaboration among PhD students, postdocs, and master’s students; and prioritising the development of innovative, biologically grounded methods over rushed deliverables for third-party stakeholders; while actively promoting continuous training and interactions with complementary academic teams.)

Looking forward to scientific discussion with your team!

Best regards,  
**Bastien Chassagnol**