

2025-09-30

QRes - An Open-Source Dose–Response Data Platform for the R Community

Viera Kovacova 

Viera Kovacova, Institute for Biological Physics, University of Cologne, Cologne, Germany

Executive Summary

Dose–response data are fundamental to research in microbiology (Lukačšínová, Fernando, and Bollenbach 2020), oncology (Kuosmanen 2021), pharmacology (Bretz, Bornkamp, and Dumortier 2025; Wang et al. 2020), biophysics (Petrungaro et al. 2025), and toxicology (Lukačšín and Bollenbach 2019). Yet raw datasets remain fragmented, inconsistently formatted, and often lack metadata, making them difficult to integrate into reproducible R workflows. Frequently, raw measurements are not shared at all, with only fitted curves or summary metrics (such as IC_{50}/OD) reported—sometimes based on methods inappropriate for the underlying data (Bayer et al. 2023; Wang et al. 2020).

In practice, raw dose–response data are stored in **small plain-text files reporting time and measured values**. Even for large-scale, parallelized experiments recorded on robotic systems over several weeks, these files rarely exceed **1 MB in size**, making them highly portable and easy to archive. When available, raw time-resolved growth data enable robust model benchmarking, transparent comparison of analytical methods, and reproducibility across studies. Beyond replication, curated raw datasets open the door to predictive modeling of evolutionary dynamics and treatment outcomes (Kuosmanen 2021; Angaroni 2025), offering a unique opportunity to accelerate both fundamental discovery and translational applications.

The **Qres platform** is an open-access dose–response database and web service hosted at the **University of Cologne**. Qres is designed to transform how raw microbial and cancer cell growth curve data are collected, curated, and analyzed. By centralizing access and standardizing analysis, Qres will speed up progress in understanding resistance dynamics and cellular responses under perturbation. This proposal requests R Consortium support to expand Qres from its current use within **CRC1310: Predictability in Evolution** to a fully R-integrated, open-source resource accessible to the global R community and beyond.

The project will deliver:

- A **public API** and an **R package** (**QresR**) for standardized data access, database storage, and

analysis.

- An **enhanced R Shiny interface** to upload and download raw data with metadata, validate new datasets, and enable interactive visualization and analysis directly in the browser.
- **Integration of predictive tools** developed in Python by Prof. Ville Mustonen, FiMAR and in Julia by Dr. Fernanda Pinheiro, Human Technopole, Milan, enabling cross-language interoperability.
- Incorporation of the **DGrowthR package** (Feldl and Olayo Alarcon 2025) developed at Helmholtz Munich as an analysis option for bacterial growth data.

Key outputs include an R package released on CRAN, standardized data formats, reproducible workflows, and community guidelines establishing **best practices and gold standards** for dose-response experiments. All analytical tools developed within Qres will be **species agnostic**, ensuring applicability across microbes, cancer models, pharmacological assays, and toxicology screens. By bridging R with Python and Julia tools, Qres will provide a foundation for AI-driven analysis and long-term reproducible science. This project directly addresses the R Consortium’s mission by strengthening technical infrastructure, fostering interoperability, and serving a broad international user base across biology, biophysics, and medicine.

The requested budget of **€50,000** will be used entirely for direct project development: a part-time developer for database and API design, a student assistant for metadata curation and testing, limited infrastructure costs, and targeted consultancy to optimize code and workflows. The PI does not request salary support, ensuring that all funds directly advance infrastructure for the R community.

Signatories

This section summarizes the individuals and groups who support, contribute to, or have been consulted on the Qres proposal. The project is already embedded in large research networks: CRC1310: Predictability in Evolution, University of Cologne, FiMAR: Finnish Centre of Excellence in Antimicrobial Resistance Research, Human Technopole, Milan, CRC1678: Systems-level consequences of fidelity changes in mRNA and protein biosynthesis, Helmholtz Munich).

Project team

- **Viera Kováčová, PhD** (viera.kovacova@uni-koeln.de) – Principal Investigator. Leads the development of Qres, supervises technical and scientific progress, and coordinates collaborations.
- **Prof. Michael Lässig** (lassig@uni-koeln.de) – Director of CRC1310. Provides strategic oversight and advice on the broader scientific vision.
- **Stephan Kleinboltig** (kleinboltig@uni-koeln.de) – CRC1310 project manager. Supports administrative coordination and R server infrastructure at the University of Cologne.
- **Part-time Developer (0.5 FTE, to be hired)** – Specialist in database and API development. Will co-design the Qres database schema, implement the public API, and ensure efficient system architecture.
- **Student Assistant (Data Steward, to be hired)** – Supports metadata curation, testing of submission workflows, and validation of Shiny interface features.

Contributors

- Prof. Ville Mustonen (FiMAR, Helsinki) – Provides predictive modeling expertise, helps shape the scientific scope, and engages international collaborators to contribute datasets.
- Dr. Fernanda Pinheiro (Human Technopol, Milan) – Leads development of the Kinbiont Julia package for bacterial growth modeling; collaborates on integration into Qres.
- Prof. Tobias Bollenbach (CRC1310, University of Cologne) – PI producing large-scale dose–response datasets; supports data contribution and benchmarking.

Consulted

1. **Colleagues and mentors** – contributing feedback, expert opinion, and testing:
 - Theresa Finke, PhD candidate, University of Cologne
 - Leon Sieger, PhD candidate, University of Cologne
 - Dr. Gabriela Pertungaro, University of Cologne ([Petrungaro et al. 2025](#))
 - Dr. Rotem Gross ([Gross et al. 2024](#))
 - Dr. Fabrizio Angaroni ([Angaroni 2025](#))
 - Medina Feldl, PhD candidate, Helmholtz, Munich – Developer of the DGRowthR package ([Feldl and Olayo Alarcon 2025](#)); contributes to Qres integration for bacterial dose–response analysis.
 - Prof. Andreas Beyer (andreas.beyer@uni-koeln.de) – Director of CRC1678; advises on systems biology integration and data-driven approaches.
 - Prof. Miroslav Baránek (Mendel University, Lednice, Czech Republic) – Provides perspective on dose–response measurements in plant pathogens.
2. **C3RDM and ITCC departments, University of Cologne** – consulted on IT infrastructure, data management, and server support.
3. **Industry contacts** – representatives from Agilent, Tecan, Molecular Devices, Promega, and BMGLabtech, who provided test/sample files from microplate readers and laboratory robots to inform data ingestion pipelines.

Community Support

The project is known and endorsed within CRC1310 (all PIs listed at [Area A](#)). This broad base of support ensures that Qres is well-positioned for adoption and sustainability, with immediate access to diverse microbial dose–response datasets.

The Problem

Dose–response measurements are among the most fundamental experiments in biology: they quantify how cells, microbes, and tissues respond to drugs, antibiotics, toxins, or environmental perturbations. These data are critical for understanding microbial resistance, cancer treatment response, and pharmacological efficacy. Despite their central role, the raw growth curve data underlying dose–response studies remain fragmented, inconsistently reported, and difficult to reuse.

Who it affects:

1. Experimental researchers face difficulties identifying optimal concentrations or conditions because raw data are buried in supplementary materials or inaccessible formats.
2. Modelers and computational biologists cannot easily benchmark or parameterize models due to lack of standardized, cross-study datasets.
3. The R community has strong modeling tools (e.g. `drc`, `nlme`, `brms`) but lacks a central resource of curated datasets with reproducible access pathways.

Why it is a problem:

1. Lack of accessible raw data prevents reproducibility and cross-study comparison.
2. Metadata are often incomplete, making it impossible to assess experimental context and test the importance of parameters.
3. Absence of standards leads to inconsistent extraction of resistance traits and dose–response parameters.
4. Inappropriate or ad hoc model fitting is common, with no accepted standard for model selection or parameter estimation (Bayer et al. 2023). This not only risks misinterpretation of experimental results but also reduces the comparability of datasets. Without broadly available raw data, it is impossible to build the large, standardized data lakes needed to train and validate AI/ML tools for optimized drug management and resistance prediction (Wang et al. 2020).

These gaps collectively hinder reproducibility, slow down discovery, and prevent the R community from becoming the central hub for dose–response analysis.

What solving the problem enables:

1. Establishing the Qres platform will provide the R community with a curated, FAIR-compliant infrastructure for dose–response data.
2. Researchers will be able to upload and share raw datasets with metadata, ensuring proper citation and recognition.
3. Modelers will have standardized, comparable inputs for parameter estimation, benchmarking, and AI-driven predictions.
4. R users will benefit from integrated pipelines linking raw data to statistical and mechanistic modeling.
5. For society, Qres will deepen our understanding of microbial resistance and its evolution, support better-informed strategies to combat antibiotic and drug resistance, and provide benchmarks that improve the design of therapeutic interventions. By enabling systematic cross-study comparisons, Qres will help identify resistance patterns earlier, guide clinical and experimental decisions, and ultimately contribute to public health.

Existing work:

1. R packages such as `drc` (Ritz et al. 2015), `nlme` (Pinheiro and Bates 2023), and `brms` (Bürkner 2017) support flexible model fitting, but they assume users already work with curated datasets and provide no infrastructure for raw data management.
2. **DGrowthR** (Helmholtz Munich) (Feldl and Olayo Alarcon 2025) enables bacterial growth curve analysis in R, but does not provide access to standardized raw data repositories.

3. **Kinbiont** (Julia) ([Angaroni 2025](#)) implements growth-curve fitting and predictive modeling, and **bmdrc** (Python) ([Degnan 2025](#)) provides benchmark dose-response analysis, but both are standalone packages without direct integration into R workflows.
4. Foundational models of microbial growth go back to **Monod (1949)** ([Monod 1949](#)), underscoring that dose-response analysis has been a central theme in biology for decades. Yet despite this long history, there is still no shared platform for raw data curation, standardized metadata, and interoperable analytical pipelines.

To date, there is no centralized, open-access platform in R that combines data storage, metadata standards, reproducible access, and interactive visualization. This gap limits reproducibility, slows the pace of discovery, and prevents the R community from fully supporting the next generation of data-driven microbiology and pharmacology.

The proposal

Approach and Work Plan

We will address the problem of fragmented and inaccessible dose-response datasets by developing Qres into an open, standardized, R-integrated platform with the following concrete actions:

API and Database Development (Months 1–4)

- **Part-time developer (0.5 FTE):** implement a REST API with standardized JSON schema, under guidance from the PI and with consultant code review.
- **Student assistant:** begin collecting and formatting test datasets with metadata for ingestion.
- Expand the database schema to store raw growth curves and curated metadata.
- Establish FAIR-compliant pipelines for data ingestion.

R Package (Months 5–6)

- **PI:** develops the open-source R package (QresR) with support from the part-time developer.
- Provide functions for data preprocessing, extraction of resistance traits, and integration with existing modeling packages (*drc*, *nlme*, *brms*).
- Begin integration of **DGrowthR** for bulk growth curve analysis.

Shiny Interface and Submission Form (Months 7–8)

- **PI:** leads development of the Shiny modules, with the student assistant testing and curating submissions.
- Extend the existing Shiny prototype into a full interface supporting upload and download of raw growth data with metadata.
- Implement automated submission validation and error reporting.
- Add interactive visualization and curve-fitting modules.

Cross-Language Integration (Months 9–10)

- Reimplement or wrap selected Python/Julia predictive tools developed by collaborators (Musterinen, Pinheiro).
- Benchmark results across platforms to ensure reproducibility.

Testing, Standards, and Dissemination (Months 11–12)

- Pilot test data submissions with internal and external collaborators.
- Optimize submission form and analysis workflows.
- Publish the R package on CRAN, complete documentation, tutorials, and case studies.
- Release community guidelines establishing gold standards for dose–response experiments.

Lean development model: The PI (Viera Kováčová) will co-develop the R/Shiny code, supported by a part-time developer (0.5 FTE) responsible for database and API implementation, and a student assistant acting as data steward for metadata curation and testing. External consultants will provide targeted mentoring and code review to optimize workflows.

Risk Management

1. **Data heterogeneity** → Mitigation: enforce a standardized metadata schema and automated validation in the Shiny submission form.
2. **Integration complexity of Python/Julia tools** → Mitigation: begin with a small subset of methods and provide R wrappers before attempting full reimplementations, with consultant support.
3. **Limited adoption** → Mitigation: leverage [CRC1310](#), [FiMAR](#), and [Human Technopole](#) networks to ensure early use and dataset contributions; provide persistent identifiers for proper citation.

Timeline

Months	Milestones
1–4	Database schema finalized; REST API prototype; test datasets curated; FAIR-compliant ingestion pipeline established.
5–6	QresR R package prototype released on GitHub; functions for data access and preprocessing; begin DGRowthR integration.
7–8	Shiny submission system extended: upload/download with metadata validation; visualization and curve-fitting modules implemented.
9–10	Cross-language integration: selected Python (FiMAR) and Julia (Human Technopole) tools wrapped/reimplemented in R; reproducibility benchmarking.
11	Pilot testing with CRC1310, FiMAR, and Helmholtz datasets; optimization of submission workflows.
12	CRAN release of QresR; full documentation, tutorials, case studies; community guidelines published.

Overview

The Qres platform is an open-access dose-response database and web service that collects, organizes, and analyzes raw, time-resolved microbial growth curves under antibiotic, genetic, and environmental perturbations. Currently, raw dose-response data are fragmented, inconsistently reported, and often hidden in supplementary files, making it difficult for researchers to reproduce analyses, perform cross-study comparisons, or build robust models of microbial resistance and cancer evolution.

Qres directly addresses this problem by providing the R community with a standardized, open-source infrastructure for dose-response data. The platform combines a robust database and public API, an R package (QresR) for reproducible workflows, and an extended Shiny interface that enables both upload and download of raw data with curated metadata, along with interactive visualization and analysis.

The project is developed under a **lean staffing plan** (PI + part-time developer + student assistant, plus targeted consultancy) and in collaboration with international partners:

- Predictive and analytical tools from [FiMAR, Helsinki](#) and [Human Technopole, Milan](#) will be reimplemented or wrapped for integration into R.
- The [DGRGrowthR package \(Feldt and Olayo Alarcon 2025\)](#) (Helmholtz, Munich) will be incorporated for bacterial growth curve analysis.

Benefits to the R community:

- Access to curated, FAIR-compliant raw dose-response datasets.
- Reproducible workflows for microbial growth, cancer cell growth, and resistance modeling.
- Integration of cross-language predictive tools into R.
- Community guidelines establishing gold standards for dose-response data.

By solving the accessibility and reproducibility gap in dose-response research, Qres will accelerate discovery, improve experimental design, and expand R's role as the central platform for quantitative biology (e.g., antibiotic resistance research).

Detail

Minimum Viable Product

The smallest version of Qres that delivers value to the R community will include:

1. A database + REST API for storing and retrieving standardized dose-response datasets.
2. An R package (QresR) providing functions to query the API and return data in tidy formats for downstream analysis with packages like *drc*, *nlme*, and *brms*.
3. A basic Shiny interface that allows users to upload raw growth curve data with metadata, validates submissions, and enables download of standardized datasets.

This MVP ensures that from the beginning, R users can both contribute new datasets and reuse existing data in reproducible workflows.

Architecture

At a high level, the architecture will consist of:

1. **Database Layer** – stores raw growth measurements, curated metadata, and derived resistance traits; implements FAIR-compliant schemas with persistent identifiers.
2. **API Layer** – RESTful API (JSON-based) for standardized programmatic access; enables both

raw data retrieval and derived parameter queries.

3. **R Package (QresR)** – provides functions to query the API, clean and preprocess data, and connect to modeling packages; interfaces with external tools such as DGRrowthR.
4. **Web Interface (Shiny)** – supports upload of raw data + metadata via automated submission form; performs validation, error reporting, and visualization of fitted curves; allows users to explore and download datasets interactively.
5. **External Tool Integration** – wrappers or reimplementations for Python/Julia

Project plan

Start-up phase

Collaboration platform: We will host all code on GitHub under an open repository (qres-platform), including the API, Shiny interface, and R package. Issues and pull requests will be used to manage contributions from collaborators and the community.

License decisions: All code will be released under the MIT license; data schemas and metadata standards will be released under CC-BY 4.0 to maximize reuse.

Reporting framework: We will provide quarterly progress updates to the ISC, including blog posts summarizing milestones. The GitHub repository will include a project board to track deliverables.

Technical delivery

The project will be delivered in phased milestones over 12 months, with work shared between the PI (R/Shiny development), a part-time developer (database and API expertise), a student assistant (data curation and testing), and external consultants (mentorship and optimization).

- **Months 1–2:**
 - Hire part-time developer and student assistant.
 - Define database schema and metadata standards.
 - Set up GitHub repository with open license and contribution guidelines.
 - Begin API blueprint under developer’s guidance.
- **Months 3–4:**
 - Developer: implement core database backend and initial API endpoints.
 - PI: create skeleton of the QresR package to connect to API.
 - Student assistant: curate test datasets and metadata.
 - First internal prototype of Shiny data upload form.
- **Months 5–6:**
 - Release alpha version of QresR package on GitHub.
 - Developer: extend API functionality and documentation.
 - PI: integrate Shiny form with API for validation.
 - Student assistant: test metadata submission workflows.
- **Months 7–8:**
 - Extend Shiny interface with interactive visualization modules.
 - Enable validated external test submissions.

- Consultants: provide code review and mentoring on API efficiency and R optimization.
- **Months 9–10:**
 - Integrate DGRowthR workflows for bulk growth analysis.
 - Provide R wrappers for selected predictive tools (Python/Julia) with consultant guidance.
 - Student assistant: continue testing with real CRC1310/FiMAR datasets.
- **Months 11–12:**
 - Community testing with CRC1310, FiMAR, and Helmholtz partners.
 - Finalize CRAN release of QresR package with vignettes.
 - Publish guidelines/white paper on dose–response data standards.
 - Disseminate results via R Consortium blog and community channels.

Other aspects

Licensing: Code under MIT; data standards and metadata under CC-BY 4.0.

Hosting: Public GitHub repository with issue tracking and contribution guidelines; Shiny app hosted on University of Cologne’s R Shiny server.

Dissemination:

1. Announcement blog post on R Consortium blog at project start.
2. Quarterly blog updates on progress.
3. Delivery blog post on release of QresR (CRAN).
4. Presentations at UseR! 2026, ISC meetings, and relevant microbiology and drug resistance conferences.
5. Social media announcements (via CRC1310, FiMAR, and partner institutes).

Budget & Funding Plan

Budget Justification

The requested funding will be used entirely for direct project development, with a focus on delivering a functional, open-source Qres platform within 12 months. We propose a lean model: a part-time developer to co-implement the database and API, a student assistant to support data stewardship and testing, and limited funds for infrastructure and expert consultancy. The PI, Viera Kováčová, will lead the project and contribute actively to programming (R/Shiny interface, metadata submission form, R package), while also receiving mentorship from the funded developer and consultants to strengthen her expertise in database and API design. No PI salary support is requested.

Item	Estimated Cost (€)	Notes
Part-time Developer (0.5 FTE, 8–10 months)	32,000	Skilled in database/API development; designs backend, mentors PI on best practices
Student Assistant (Data Steward, 8h/week, 12 months)	6,000	Supports metadata curation, data validation, Shiny testing

Item	Estimated Cost (€)	Notes
Miscellaneous / Infrastructure	2,000	Server extensions, additional storage, small-scale shinyapps.io environment for testing
Consultancy / Mentorship	10,000	Contracted expert(s) from the R community for regular guidance on code optimization, database design, and API best practices
Total	50,000	

Milestones linked to funding

Funding is requested primarily for labor costs:

Month(s)	Deliverable / Milestone	Funding (€)
2	Database schema + REST API prototype; initial test datasets curated	10,000
4	Extended database + FAIR ingestion pipeline; API documentation draft	10,000
6	QresR R package prototype on GitHub; DGrowtHR integration started	10,000
8	Shiny submission system with metadata validation + visualization modules	10,000
12	CRAN release of QresR; tutorials, case studies, community guidelines	10,000
Total		50,000

Notes / Flexibility

1. The Consultancy/Mentorship line (€10k) can be adjusted downward (e.g. €5–7k) if reviewers push back on budget.
2. University of Cologne will provide an additional student assistant (in-kind contribution, not funded by ISC).
3. No overhead, travel, or PI salary is requested.

Success

Definition of done

The project will be considered complete and successful when:

1. The Qres database and REST API are fully operational, allowing storage and retrieval of dose–response datasets with curated metadata.
2. The QresR package is publicly released on CRAN and GitHub, enabling R users to programmatically query, preprocess, and analyze datasets.
3. The Shiny interface supports automated data submission (with validation) and interactive download/visualization of raw data and fitted models.
4. Integration with external predictive tools (Kinbiont Julia ([Angaroni 2025](#)), DGGrowthR ([Feldl and Olayo Alarcon 2025](#)) and *bmdrc* Python ([Degnan 2025](#))) is demonstrated through vignettes and tutorials.
5. Community guidelines / white paper on best practices for dose–response experiments are published and disseminated.

Measuring success

Success will be measured using concrete, trackable outputs:

1. Technical outputs:
 - QresR package accepted on CRAN.
 - API documentation publicly available.
 - Shiny interface deployed with submission/download capability.
2. Community uptake:
 - At least 5 external datasets submitted and validated through the automated submission system.
 - Engagement of early adopters from:
 - CRC1310: Predictability in Evolution, University of Cologne
 - FiMAR: Finnish Centre of Excellence in Antimicrobial Resistance Research
 - Human Technopole, Milan
 - Helmholtz Munich – Helmholtz Zentrum München
3. Dissemination:
 - Release of at least 2 vignettes/tutorials demonstrating workflows in R.
 - Publication of guidelines for dose–response data management and modeling.

Future work

Once Qres reaches full functionality, we will prepare a high-impact publication describing its architecture, features, and scientific use cases. The manuscript will highlight:

- The need for standardized, FAIR-compliant dose–response data.
- Qres infrastructure (database, API, R package, Shiny interface).
- Integration of predictive tools across R, Python, and Julia.
- Demonstration datasets from microbial resistance and cancer evolution.
- Benchmarks comparing automated analysis pipelines (e.g., DGR, Kinbiont).

Target journals could include Nature Biotechnology, Nature Communications, Nucleic Acids Research (Database issue), or Bioinformatics. This publication will provide a citable reference for Qres, ensuring that dataset contributors receive recognition and that the platform is embedded in the global research ecosystem.

- Angaroni, Peruzzi, Fabrizio. 2025. “Translating Microbial Kinetics into Quantitative Responses and Testable Hypotheses Using Kinbiont.” *Nature Communications* 16 (6440). <https://www.nature.com/articles/s41467-025-61592-6#citeas>.
- Bayer, Franziska, Torben Griebel, Luca Borger, and Tobias Bollenbach. 2023. “Comparing Methods to Estimate Growth Parameters from Microbial Growth Curves.” *Nature Communications* 14 (362): 1–13. <https://doi.org/10.1038/s41467-023-43696-z>.
- Bretz, Frank, Björn Bornkamp, and Thomas Dumortier. 2025. “Dose-Response Characterization: A Key to Success in Drug Development.” *Clinical Trials* 22 (4): 384–92. <https://doi.org/10.1177/17407745251350289>.
- Bürkner, Paul-Christian. 2017. “Brms: An r Package for Bayesian Multilevel Models Using Stan.” *Journal of Statistical Software* 80 (1): 1–28.
- Degnan, Lisa M. AND Truong, David J. AND Bramer. 2025. “Bmdrc: Python Package for Quantifying Phenotypes from Chemical Exposures with Benchmark Dose Modeling.” *PLOS Computational Biology* 21 (7). <https://doi.org/10.1371/journal.pcbi.1013337>.
- Feldl, Medina, and Roberto Olayo Alarcon. 2025. *DGR: Bacterial Growth Curve Analysis*. <https://bio-datascience.github.io/DGR/>.
- Gross, Rotem, Muhittin Mungan, Suman G. Das, Melih Yüksel, Berenike Maier, Tobias Bollenbach, Joachim Krug, and J. Arjan G. M. de Visser. 2024. “Collective β -Lactam Resistance in *Escherichia Coli* Due to β -Lactamase Release Upon Cell Death.” *bioRxiv*. <https://doi.org/10.1101/2024.10.14.618215>.
- Kuosmanen, Johannes AND Noble, Teemu AND Cairns. 2021. “Drug-Induced Resistance Evolution Necessitates Less Aggressive Treatment.” *PLOS Computational Biology* 17 (9): 1–22. <https://doi.org/10.1371/journal.pcbi.1009418>.
- Lukačičšin, Martin, and Tobias Bollenbach. 2019. “Emergent Gene Expression Responses to Drug Combinations Predict Higher-Order Drug Interactions.” *Cell Systems* 9 (5): 423–433.e3. <https://doi.org/10.1016/j.cels.2019.10.004>.
- Lukačičšinová, Marta, Booshini Fernando, and Tobias Bollenbach. 2020. “Highly Parallel Lab Evolution Reveals That Epistasis Can Curb the Evolution of Antibiotic Resistance.” *Nature Communications* 11: 3105. <https://doi.org/10.1038/s41467-020-16932-z>.
- Monod, Jacques. 1949. “The Growth of Bacterial Cultures.” *Annual Review of Microbiology* 3 (1): 371–94. <https://doi.org/10.1146/annurev.mi.03.100149.002103>.

- Petrungaro, Gabriela, Theresa Fink, Booshini Fernando, Gerrit Ansmann, and Tobias Bollenbach. 2025. "Function-Specific Epistasis Shapes Evolutionary Trajectories Towards Antibiotic Resistance." *bioRxiv*. <https://doi.org/10.1101/2025.07.09.663857>.
- Pinheiro, José, and Douglas Bates. 2023. *Mixed-Effects Models in s and s-PLUS*. Springer.
- Ritz, Christian, Florent Baty, Jens C Streibig, and Daniel Gerhard. 2015. "Dose-Response Analysis Using r." *PLOS ONE* 10 (12): e0146021.
- Wang, Dennis, James Hensman, Ginte Kutkaite, Tzen S Toh, Ana Galhoz, GDSC Screening Team, Jonathan R. Dry, et al. 2020. "A Statistical Framework for Assessing Pharmacological Responses and Biomarkers Using Uncertainty Estimates." *eLife* 9: e60352. <https://doi.org/10.7554/eLife.60352>.