

RAFAEL CARLOS REDING ROMAN

Senior Research Associate, University of Bristol

School of Cellular and Molecular Medicine
Faculty of Life Sciences, University of Bristol
Bristol, BS8 8DZ, United Kingdom.

Contact: carlos.reding@bristol.ac.uk
Website: <https://rc-reding.gitlab.io/>
Code:
https://git.disroot.org/rc_reding/
<https://gitlab.com/rc-reding/>

APPOINTMENTS

2022 – 2023 SENIOR RESEARCH ASSOCIATE. Faculty of Life Sciences, University of Bristol (UK).

Building surveillance capacity to monitor antibiotic-resistant mutants using whole-genome sequencing datasets. The core of this project is the 'Hound', a user-friendly bioinformatic tool that I wrote to analyse prokaryote genomes without relying on reference genomes. Three core features of 'Hound' are I) the estimation of copy number of genes of interests, II) analysis of sequences upstream of the coding sequence (i.e. promoter mutations), and III) sorting and merging contigs in *de novo* assemblies. I have screened nearly 6,700 isolates from the Avison laboratory so far within 12 months, detecting mutations not picked up by reference-aided tools such as ResFinder, helping members of the laboratory boost their research. Training of the Avison's laboratory on the use of this tool.



Principal Investigator: Prof Matthew Avison.

2020 – 2021 POSTDOCTORAL RESEARCH FELLOW. Department of Genetics, Stanford University (USA).

Developed an affordable impedance biosensor to detect the amplification of SARS-CoV-2 RNA in bespoke biochemical assays. I liaised with electric engineers and molecular biologists to build the prototype using a 3D-printed microfluidic platform connected to a microcontroller-based evaluation board, and implemented a loop-mediated amplification assay along with the analysis pipeline in Python. I validated the design using a benchtop Zürich HF2 spectroscope. With this device I could detect the amplification of SARS-CoV-2 cDNA at the nucleotide level, with the impedance magnitude being approx. 35Ω per nucleotide added.

Principal Investigator: Prof Lars Steinmetz.

2018 – 2020 DEVELOPMENT SCIENTIST. BioDynamic Devices, Exeter (UK).

Co-developed a computer-vision spectrophotometer as part of the ERC Proof-of-Concept grant '*Microbiological fluorescence observatory for antibiotic resistance tracking*' (MuFLOART, €149,249), where **I was named post-doctoral research associate**. Here I developed early prototype of the device (breadboard circuitry, software, and biological assays) and later pre-commercial specifications. **The startup company**  **BioDynamic Devices emerged from this project** to seek commercialisation of the device. A patent is now pending for the device  (WO 2020/165582 A1).

2016 – 2020 ASSOCIATE RESEARCH FELLOW. Living Systems Institute, University of Exeter, (UK).

Designed data mining algorithms and mathematical models to study the adaptation to antibiotics in *Escherichia coli* and, particularly, the regulation of the multi-drug efflux pump AcrAB-TolC. I cross-referenced phenotypic data with whole-genome sequencing and quantitative PCR datasets to track the emergence and fate of mutations in the aforementioned bacterium. Drafted manuscripts for publications and presentations for international conferences.

Principal Investigators: Prof Robert Beardmore, Prof Ivana Gudelj.

EDUCATION

2016 PHD IN QUANTITATIVE BIOLOGY, University of Exeter, UK.

Thesis: *Ecological conditions leading to the sweep of antibiotic resistance genes in the model-type bacterium*


Escherichia coli.  <https://hdl.handle.net/10871/19693>

Supervisor: Prof Robert Beardmore.


Degree award date: 15th February 2016.

2010 LICENCIATURA EN BIOLOGÍA (5-year degree), Universidad de Málaga, Spain.



PATENTS

2020  **WO 2020/165582 A1** — **Light Modulation (LiMo®)** technology for the spatio-temporal analysis of biological samples: A high-throughput computer-vision device to incubate and measure the growth of microbial cultures in microtitre plates, with software-enabled optimisation of lighting conditions to increase detection sensitivity. **Contribution:** Designed and built early prototype, developed and implemented API and python libraries, and designed/executed the experimental protocols.

ASSOCIATED SOFTWARE




 https://git.disroot.org/rc_reding/ Server-side software, communication stack (socket), hardware control library (threading, pigpio, w1thermsensor, picamera), and stand-alone data analysis pipeline (numpy, scipy, opencv, multiprocessing) implemented as a python package (limoControl) under LGPL v2.1 license.

SOFTWARE





- 2023  <https://gitlab.com/rc-reding/pgeocode> Added support for full post codes to pgeocode, a postal code geocoding and distance calculation package for Python (commit 1d96b6a).
- 2023  <https://gitlab.com/rc-reding/software/-/tree/main/Hound> Python implementation of *Hound*—currently at version 1.0.3 released along with the preprint—under LGPL v2.1 license.

PUBLICATION LIST

PEER-REVIEWED JOURNALS

1. Carlos Reding, Naphat Satapoomin, Matthew Avison. Hound: A novel tool for the automated mapping of genotype to phenotype in bacterial genomes assembled *de novo*. *Brief. Bioinform.* (in press, DOI: [10.1093/bib/bbae057](https://doi.org/10.1093/bib/bbae057)).
 [bioRxiv 2023.09.15.557405](https://doi.org/10.1101/2023.09.15.557405) **Contributions:** I developed a novel analysis pipeline to create genetic profiles from whole-genome sequencing datasets assembled *de novo*. Hound finds mutations in a user-given gene of reference, including promoter and gene copy number. **Significance:** One of the [very] tools for the extensive detection of mutations in *de novo* assemblies, respecting within species microbial genetic heterogeneity and facilitating the detection of *any* designated gene—can be applied beyond AMR—and mutations that may increase gene expression.  **Code available in my gitlab repository.**
2. Oliver Mounsey⁺, Laura Marchetti⁺, Julián Parada⁺, Laura V. Alarcón, Florencia Aliverti, Matthew B. Avison, Carlos S. Ayala, Cristina Ballesteros, Caroline M. Best, Judy Bettridge Andrea Buchamer, Daniel Buldain, Alicia Carranza, David Demeritt, María Paula Escobar, Lihuel Gortari Castillo, David Griffo, Maite Corti Isgro, María Jaureguiberry, Mariana F. Lucas, Federico Luna, L. Vanina Madoz, Hernán D. Nievas, Marco A. Ramirez, Carlos Reding, Kristen K. Reyher, Lucy Vass, Sara Williams, José Giraudo, R. Luzbel De La Sota, Nora Mestorino, Fabiana A. Moredo, Matías Pellegrinos. (2023). Genomic epidemiology of third-generation cephalosporin-resistant *Escherichia coli* from Argentinian pig and dairy farms reveals animal-specific patterns of co-resistance and resistance mechanisms. *Appl. Environ. Microbiol.*, **90**(1) e01791-23 (2024). **Contributions:** I used a bespoke software (Hound) to screen through all the isolates analysed, and retrieve the sequences of multiple blaCTX-M genes and promoter sequence of *ampC* to infer their likely resistance to third-generation cephalosporin (3GC). **Significance:** Little is known about the ecology of AMR among opportunistic human pathogens on South American farms. This study, the largest to date, found *E. coli* isolates resistant to 3GC, florfenicol, and amoxicillin/clavulanate in pigs and dairy cattle.
3. Carlos Reding. (2022). Predicting the re-distribution of antibiotic molecules caused by inter-species interactions in microbial communities. *ISME Commun.* **2**, 110. **Significance:** Simple physical laws can help predict the change in drug efficacy observed between pure and mixed culture conditions, suggesting I) that drug efficacy can be predictably manipulated, and II) a simple mechanism to explain the emergence of co-operation in prokaryotes.  **Code available in my gitlab repository.**
4. Carlos Reding, Pablo Catalán, Gunther Jansen, Tobias Bergmiller, Philip Rosenstiel, Hinrich Schulenberg, Robert Beardmore (2021). The Antibiotic Dosage of Fastest Resistance Evolution: gene amplifications underpinning the inverted-U. *Mol. Biol. Evol.*, msab025. **Contribution:** Designed and performed experiments, wrote phenotypic and genomic data analysis pipeline, wrote the manuscript. **Significance:** Underpins the relationship between antibiotic concentration and speed of adaptation.
5. C. Reding-Roman, S. Duxbury, M. Hewlett, F. Gori, I. Gudelj and R. Beardmore. (2017). The unconstrained evolution of fast and efficient antibiotic-resistant bacterial genomes. *Nat. Ecol. Evol.* **1**, 0050. **Contribution:** Designed and performed experiments, wrote phenotypic and genomic data analysis pipeline, wrote the manuscript. **Significance:** Despite its sound foundations, *rK selection theory* fell out of favour given the conflict between data and theory. Here we solve this conflict and show why growth rate (*r*) and population size (*K*) may trade-off, trade-up, or not be correlated at all.
6. A. Fuentes-Hernandez, J. Plucain, F. Gori, R. Peña-Miller, C. Reding, G. Jansen, H. Schulenberg, I. Gudelj, and R. Beardmore. (2015). Using a Sequential Regimen to Eliminate Bacteria at Sub-Lethal Antibiotic Dosages. *PLoS Biol.* **13**(4):e1002104. **Contribution:** Calibration of optical density vs cell number, replicated experiments in Figures 4 and 5. **Significance:** Here we show that, contrary to conventional wisdom, bacterial cultures can be fully inhibited using sub-lethal drug combinations through mathematically-driven regimens.
7. R. Peña-Miller, A. Fuentes-Hernandez, C. Reding, I. Gudelj and R. Beardmore. (2014). Testing the optimality properties of a dual antibiotic treatment in a two-locus, two-allele model. *ř. R. Soc. Interface* **11**:20131035. **Contribution:** Evolutionary experiment to validate theoretical prediction when one drug (erythromycin) is used, analysed data. **Significance:** Here we show that optimal antibiotic therapies are those that change over time, outperforming those that are use the same drug/dose periodically.
8. Antonio Jiménez, Diana Boomgard, Patricia Rivera, C. Reding, José M. Pérez-Fígares. (2005). Degeneración retiniana asociada a hidrocefalia congénita debida a mutación en el gen que codifica alfa-SNAP. *Rev. Neurol.* **41** (S02): 64. **Contribution:** As an undegrad student, I processed brain tissue samples using a microtome, and hematoxylin and eosin staining. **Significance:** Here we explore the contribution of α -SNAP protein to congenital hydrocephaly in mice.


PREPRINTS ARCHIVE

1. Punyawee Dulayangkul, Jordan E Sealey, Winnie WY Lee, Carlos Reding, Kate J Heesom, Naphat Satapoomin, Philip B Williams, Matthew B Avison. Improving nitrofurantoin resistant prediction in *Escherichia coli* from whole genome sequence by integrating NfsA/B enzyme assays. (**undergoing peer-review in *Journal of Clinical Microbiology***)  [bioRxiv 2024.01.25.577238](https://doi.org/10.1101/2024.01.25.577238). **Contribution:** I processed 200 *E. coli* urine samples using the Hound pipeline to find variations in *nfsA* and *nfsB* copy number, as well as mutations in the coding sequence. **Significance:** Nitrofurantoin is the first choice for treatment of uncomplicated urinary tract infections in the UK. Resistance to this antibiotic is caused by loss-of-function (LoF) mutations in *nfsA* and *nfsB*. Here we combined whole-genome sequencing, proteomics, and enzyme assays to identify mutations that cause LoF mutations in *E. coli* urine samples.
2. Carlos Reding. Plasmid carriage and the unorthodox use of Fisher's theorem in evolutionary biology (**undergoing peer-review in *PNAS Nexus***).  [bioRxiv 810259](https://doi.org/10.1101/2024.01.25.577238). **Significance:** This study shows that fitness can change through time without mutations leading to the erroneous conclusion that fast-reproducing genotypes necessarily outcompete those reproducing slower. It also exposes conditions where fast- and slow-growing genotypes can be co-maintained, helping understand the seemingly-paradoxical abundance of plasmids in nature.  **Code available in my gitlab repository.**
3. Carlos Reding⁺, Mark Hewlett⁺, Tobias Bergmiller, Ivana Gudelj, Robert Beardmore. Imaging Fisher travelling waves in antibiograms: emergence of antibiotic-resistance patterns.  [bioRxiv 806232](https://doi.org/10.1101/2024.01.25.577238). **Contribution:** Co-developed device, wrote image analysis algorithm, performed experiments, data analysis, and wrote manuscript. **Significance:** Here we show that antibiotics create reservoirs of carbon, promoting the rapid (<24h) onset of drug-resistant mutants. We also monitored in real-time the formation and change of the resulting Fisher's travelling wave.

GRANTS, AWARDS & RECOGNITIONS

SUCCESSES

- 2018 **ERC Proof-of-Concept Grant** 'Microbiological fluorescence observatory for antibiotic resistance tracking' (MuFLOART) with me as PDRA, with Profs Ivana Gudelj and Robert Beardmore as principal investigators (€ 149,249). **Contributions:** I helped write the specifications of the device in the grant, as well as the experimental protocol used to validate the pipeline, and costing of the components.
- 2017 University of Exeter *Above & Beyond* Recognition for excellent contributions from postdocs to teaching and widening participation (included £250 as a gift).
- 2015 London Mathematical Society **Travel Grant** for Early Career Researchers (£102).

NEAR-SUCCESSSES —  THAT'S LIFE...

- 2022 **Royal Society University Research Fellowship** URF\R1\231680: *Modelling the basic principles governing ribosomal gene regulation* (£1,667,120 over 8 years). **Shortlisted for independent review in January 2023**—Not funded following second round of review.
- 2022 **Medical Research Council Career Development Award** MR/X020738/1: *Modelling the effect of antibiotics and plasmid carriage on the regulation of ribosomal genes in bacteria* (£1,280,585 over 5 years).
- 2021 **Royal Society University Fellowship** 'Negative cultures to detect and sequence un-cultivable soil microorganisms' URF\R1\221058 with Prof Pietro Ciuta at Cavendish Laboratory, University of Cambridge (UK, £145,000 per year inc. salary, 5-year appointment).
- 2018 **BBSRC Discovery Fellowship** 'Ecological mechanisms that control antibiotic sensitivity during polymicrobial infections' BB/S010653/1, with Profs Simon Foster and Michael Brockhurst at University of Sheffield (UK, £375,000).
- 2018 **EPSRC Standard Grant** 'Engineering a data analysis platform that quantifies antibiotic and phage resistance during sepsis treatment' ES/T016124/1, with Profs Robert Beardmore and Ivana Gudelj as co-PI at University of Exeter (UK), and me as researcher co-investigator (approx. £685,000).

INVITED TALKS, POSTERS & CONFERENCES

- SETP. 2023 *IOI Interdisciplinary Approaches to AMR* Conference held in the Ineos-Oxford Institute, University of Oxford, UK (poster)—**Temporarily delayed due to RAAC being found in the venue.**
- AUG. 2023 *MicrobesNG POP UP* Conference, held in University of Manchester, UK (Contributed talk).
- JUNE 2023 School of Cellular and Molecular Medicine at the University of Bristol. Invited talk hosted by Dr Yuiko Takebayashi.
- MAY 2023 Science communication event *Pint of Science* (Bristol, UK). Invited by Will Miller—'Our Body' event manager—to talk in the theme *microbes and antibiotic resistance*.
- MAY 2021 Presentation at "Bug Club", held in the Department of Biology at Stanford University. Invited by Prof Ami Bhatt, MD and Prof Sharon Long.

- OCT. 2019** Department of Environmental Systems Science, ETH Zürich, Switzerland. Invited talk hosted by Prof Martin Ackermann. Zürich, Switzerland.
- SEPT. 2018** Westmead Hospital, Sydney, Australia. Invited talk hosted by Prof Jonathan Iredell.
- MARCH 2018** *Floreys Institute Seminar Series*. University of Sheffield, UK. Invited by Prof Simon Foster.
- APRIL 2017** *Gene Expression and Synthetic Biology Workshop*. University of Exeter, UK (Contributed talk).
- SEPT. 2017** *Mathematical Challenges from Life Sciences*. University of Warwick, UK (Contributed talk).
- MAY 2017** *Applied Bioinformatics & Public Health Microbiology*. Wellcome Genome Campus, Hinxton, UK (poster).
- DEC. 2015** *Third International Biannual Evolution & Cancer Conference (IBECC): Evolutionary Tradeoffs & Clinical Consequences*. University of California San Francisco, USA (Contributed talk).
- APRIL 2015** *Modelling Biological Evolution*. University of Leicester, UK (poster).
- JUNE 2014** *BioDynamics Workshop*, College of Engineering Mathematics and Physical Sciences. University of Exeter, UK (Contributed talk).
- MAY 2014** *Systems Biology of Drug Resistance Evolution*, Centre for Genomic Sciences, UNAM. Cuernavaca, Mexico (Contributed talk).
- SEPT. 2005** *XI Congress of the Spanish Society of Neuroscience*, University of Málaga, Málaga, Spain (poster).

TEACHING EXPERIENCE

UNIVERSITY OF BRISTOL


- 2022–PRESENT** Tutorial leader in the **undergraduate** course *Cellular and Molecular Pathology*. (Winter & Spring terms).

UNIVERSITY OF EXETER

- 2011 – 2015** Graduate Teaching Assistant and demonstrator in the **undergraduate** course *Fundamental Principles, Research Skills & Bioethics*. (Winter term.)
- 2011 – 2015** Demonstrator in the **undergraduate** course *Modern Theories of Evolution*. (Winter term).
- 2011 – 2015** Graduate teaching assistant and demonstrator in the **undergraduate** course *Evolution & Informatics*. (Spring term).
- 2011 – 2015** Statistics tutor and demonstrator in the **undergraduate** course *Genetics*. (Winter term)
- 2012 – 2013** Graduate teaching assistant in the **postgraduate** course MSc Sequence Analysis & Structural Bioinformatics. (Winter term).
- 2012** Instructor in the *Global Challenges Workshop* held at the University of Exeter (UK) to introduce 1st-year **undergraduate** students how bioscience research addresses current problems in society.

LEADERSHIP ACTIVITIES

MENTORING & SUPERVISION

- 2023–2024** Supervision of University of Bristol **MSci student** Finn Mansfield.
- 2023–2024** Mentoring of Michael Mazurek, 2nd year Science Research student at Fox Lane High School, New York (USA), in the design and execution of a science project about antimicrobial resistance. Student supervision by Ms. Amy Pirro (teacher). **On Jan 20th, 2024, Michael received an AWARD for his project at the Westchester-Rockland Junior Science & Humanities Symposium.**
- 2023** Mentoring of University of Bristol PhD Student Winnie Lee—PhD writing, postdoc market navigation.
- 2023** Bioinformatics training and mentoring of visiting researcher Hikmat Balogun-Abiola from Olabisi Onabanjo University (Nigeria).
- 2018** Training and supervision of Charlotte McDermott during her final-year **undergraduate** project, which included a £400 budget.
- 2017** Training and supervision of India Hatfield during her final-year **undergraduate** project, this time including a £400 budget.
- 2015–2017** Training of **PhD student** Sarah Duxbury during rK-selection project using *Candida spp.*
- 2015** Training and supervision of Edward Baggs during his final-year **undergraduate** project.
- 2015** Training and supervision of Francesca during her final-year **undergraduate** project.
- 2013–2016** Training of **PhD student** Mark Hewlett during bacteria-phage evolution project.
- 2013** Member of the organising committee of the conference  **Quantitative Evolutionary Dynamics** held in Teignmouth (UK) bringing together speakers bringing together a list of international speakers from the fields of physical biology, evolutionary biology, and systems biology studying from plant and human pathogens to natural fungal ecosystem, consortia of symbionts, and response to antibiotics the single-cell level.

OUTREACH

- 2023 Science communication event *Pint of Science* with a talk about microbes and antibiotic resistance.
- 2021 Designed a 3D printed 96-well pin replicator for a project led by Dr Magdalena Strinrück from IST Austria, where school children used pH indicator dyes to create droplet-pixelated, pH art.
- 2015 – 2017 Outreach activities in City of Stoke-on-Trent Sixth Form College in the UK (how many bacteria grow in peas, antibiotic properties of garlic, vinegar and lemon juice, and how to build a hawk-eye system with a smartphone).
- 2016 Co-organiser of the First NorthWest Science Summer School held at Staffordshire University (Stoke-On-Trent, UK).

ACADEMIC ACTIVITIES & MEMBERSHIPS

- 2024 Grant referee for the **Medical Research Council (MRC)**, UK.
- 2023 – PRESENT Member of editorial board in the journal *npj Antimicrobials & Resistance* (Springer, launched in 2023).
- 2021 – PRESENT Associate member of the **Royal Society Proceedings B Preprint Editorial Team**.
- 2021 Grant referee for the **Bio-Design and Manufacturing Journal** (Springer, 5-year IF 6.302).
- 2020 Reviewer for the **Economic and Social Research Council (ESRC)**, UK.