Jean-Baptiste Lugagne

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Education

2016 **PhD, Bioengineering**, U. Sorbonne Paris-Cité, France

Real-time control of a genetic toggle switch
Co-advised by Prof. Grégory Batt, Inria & Prof. Pascal Hersen, Cnrs.

2012 **M.S., Signal Processing Engineering**, Grenoble Institute of Technology, France

Stochastic simulation of enzymatic reactions under transcriptional feedback regulation
Co-advised by Prof. Guy-Bart V. Stan & Dr. Diego A. Oyarzún, Imperial College London.

2010 **B.S., Electrical Engineering**, Grenoble Institute of Technology, France

Research experience

2018-Present **Post-doctoral researcher**, Boston University, United States
Advisor: Prof. Mary J. Dunlop
Control theory • Deep learning • Synthetic biology • Antibiotic resistance • Metabolic engineering • Optogenetics • Microfabrication & microfluidics • Image processing

- Developed a novel approach for real-time feedback control of gene expression, including for antibiotic resistance genes, in thousands of single *E. coli* cells based on deep model predictive control and optogenetics.
- Created DeLTA, a deep learning-based software for single cell segmentation and tracking in time-lapse microscopy movies.
- Established collaboration with Prof. Ji-Xin Cheng's group for label-free stimulated Raman spectro-microscopy imaging of bioproduction in *E. coli* cells.

2012-2017 **Graduate research assistant & Post-doctoral researcher**,Cnrs & Inria, Paris, France
Advisors: Prof. Pascal Hersen & Prof. Grégory Batt
Control theory • Synthetic biology • Microfabrication & microfluidics • Automated microscopy • Machine learning • 3D printing & electronic prototyping

- Controlled gene expression in a genetic toggle switch to stabilize it around its unstable equilibrium point in single cells, with real-time feedback or dynamic forcing.
- Developed microscopy image analysis algorithm based on classification of pixel's intensity signatures in a Z-stack with support vector machines or random forests.

2012 **Graduate research assistant**, Imperial College, London, UK
Advisors: Prof. Guy-Bart V. Stan & Dr. Diego A. Oyarzún
Systems biology • Stochastic modelling of gene expression and metabolism • Control theory

- Investigated propagation of genetic and metabolic noise in a metabolic pathway under transcriptional feedback.

2011 **Graduate research assistant**, Inria, Grenoble, France
Advisor: Prof. Hidde de Jong
Systems & synthetic biology • Deterministic modelling of gene expression • Signal processing

- Modeled and fit parameters to experimental data of spatio-temporal dynamics in a colony of synthetic *E. coli* cells coupling quorum sensing and toggle switch circuits for biosensing.

Publications

†: co-corresponding author – ∗: co-first author

In revision

Lugagne, J.-B.†, Blassick, C. M., Dunlop, M. J.†(2022). Deep model predictive control of gene expression in thousands of single cells. *bioRxiv*. 10.1101/2022.10.28.514305

Published articles

Klumpe, H. E.*, **Lugagne, J.-B.***†, Khalil, A. S., Dunlop, M. J.†(2023). Deep neural networks for predicting single cell responses and probability landscapes. *ACS Synthetic Biology*. 10.1021/acssynbio.3c00203

Tague, N., Lin, H., **Lugagne, J.-B.**, O'Connor, O. M., Burman, D., Wong, W. W., Cheng, J.-X., Dunlop, M. J. (2023). Longitudinal single-cell imaging of engineered strains with stimulated Raman scattering to characterize heterogeneity in fatty acid production. *Advanced Science*. 10.1002/advs.202206519

Lugagne, J.-B., & Dunlop, M. J. (2022). Anticipating antibiotic resistance. *Science*. [Perspective] 10.1126/science.abn9969

Sampaio, N. M. V, Blassick, C. M., Andreani, V., **Lugagne, J.-B.**, & Dunlop, M. J. (2022). Dynamic gene expression and growth underlie cell-to-cell heterogeneity in Escherichia coli stress response. *PNAS*. 10.1073/pnas.2115032119

O'Connor, O. M., Alnahhas, R. N., **Lugagne, J.-B.**†, & Dunlop, M. J.†(2022). DeLTA 2.0: A deep learning pipeline for quantifying single-cell spatial and temporal dynamics. *PLOS Computational Biology*. 10.1371/journal.pcbi.1009797

Lin, H., Lee, H. J., Tague, N., **Lugagne, J.-B.**, Zong, C., Deng, F., Shin, J., Tian, L., Wong, W., Dunlop, M. J., & Cheng, J.-X. (2021). Microsecond fingerprint stimulated Raman spectroscopic imaging by ultrafast tuning and spatial-spectral learning. *Nature Communications*. 10.1038/s41467-021-23202-z

Lugagne, J.-B., Lin, H., & Dunlop, M. J. (2020). DeLTA: Automated cell segmentation, tracking, and lineage reconstruction using deep learning. *PLOS Computational Biology*. 10.1371/journal.pcbi.1007673

Lugagne, J.-B., & Dunlop, M. J. (2019). Cell-machine interfaces for characterizing gene regulatory network dynamics. *Current Opinion in Systems Biology*. 10.1016/j.coisb.2019.01.001

Lugagne, J.-B., Jain, S., Ivanovitch, P., Ben Meriem, Z., Vulin, C., Fracassi, C., Batt, G., & Hersen, P. (2018). Identification of individual cells from z-stacks of bright-field microscopy images. *Scientific Reports*. 10.1038/s41598-018-29647-5

Lugagne, J.-B., Kirch, M., Köhler, A., Batt, G., & Hersen, P. (2017). Balancing a genetic toggle switch by real-time feedback control and periodic forcing. *Nature Communications*. 10.1038/s41467-017-01498-0

Lugagne, J.-B., Brackx, G., Seyrek, E., Berret, J.-F., Hersen, P., & Charron, G. (2017), Assembly and characterizations of bifunctional fluorescent and magnetic microneedles displaying length tunability over one decade, *Advanced Functional Materials*. 10.1002/adfm.201700362

Piffoux, M., Silva, A. K. A., **Lugagne, J.-B.**, Hersen, P., Wilhelm, C., & Gazeau, F. (2017). Extracellular vesicle production loaded with nanoparticles and drugs in a trade-off between loading, yield and purity: Towards a personalized drug delivery system. *Advanced Biosystems*. 10.1002/adbi.201700044

Oyarzún, D. A., **Lugagne, J.-B.**, & Stan, G. B. V. (2014). Noise propagation in synthetic gene circuits for metabolic control. *ACS Synthetic Biology*. 10.1021/sb400126a

Lugagne, J.-B., Oyarzún, D. A., & Stan, G. B. V. (2013). Stochastic simulation of enzymatic reactions under transcriptional feedback regulation. In *IEEE European Control Conference 2013 (ECC13)*. 10.23919/ECC.2013.6669756

Research presentations

Talks

Lugagne, J.-B., Klumpe, H. E., Blassick, C. M., & Dunlop, M. J. (2023). High-throughput single-cell control using real-time feedback. *SwissUK Synbio*, Lausanne, Switzerland.

Lugagne, J.-B., & Dunlop, M. J. (2022). High-throughput single-cell control using real-time feedback. *Biocontrol seminars*, Online.

Lugagne, J.-B., & Dunlop, M. J. (2022). High-throughput single-cell control using real-time feedback. *Winter Q-Bio 2022*, Ko Olina, Hawaii, USA.

Lugagne, J.-B., & Dunlop, M. J. (2021). Deep model predictive control of gene expression in single cells. *BDC Spring Symposium*, Boston University, USA.

Lugagne, J.-B., & Dunlop, M. J. (2019). Single-cell real-time feedback control of gene expression. *BDC Symposium*, Boston University, USA.

Lugagne, J.-B.(2017). Balancing a genetic toggle switch by real-time feedback control and periodic forcing. ETH Zürich, Switzerland.

Lugagne, J.-B.(2017). Balancing a genetic toggle switch by real-time feedback control and periodic forcing. University of Edinburgh, United-Kingdom.

Lugagne, J.-B.(2017). Balancing a genetic toggle switch by real-time feedback control and periodic forcing. University of Cambridge, United-Kingdom.

Lugagne, J.-B., Kirch, M., Köhler, A., Batt, G., & Hersen, P. (2015). Real-time control of a genetic toggle switch. *Design, Optimization and Control in Systems and Synthetic Biology*, Paris, France.

Lugagne, J.-B., Oyarzún, D. A., & Stan, G. B. V. (2013). Stochastic simulation of enzymatic reactions under transcriptional feedback regulation. *IEEE European Control Conference 2013 (ECC13)*, ETH Zürich, Switzerland.

Conference posters

Lugagne, J.-B., Tague, N., & Dunlop, M. J. (2019) Single-cell, dynamic interrogation of antibiotic resistance acquisition. *Q-Bio 2019*, San Francisco, California, USA.

Lugagne, J.-B., Tague, N., & Dunlop, M. J. (2019) Dynamic control of antibiotic resistance related genes with optogenetics. *EBRC Retreat*, Boston, Massachusetts, USA.

Lugagne, J.-B., Kirch, M., Köhler, A., Batt, G., & Hersen, P. (2017). Balancing a genetic toggle switch by real-time feedback control and periodic forcing. *International Workshop on Control Engineering and Synthetic Biology*, London, United-Kingdom.

Lugagne, J.-B., Kirch, M., Köhler, A., Batt, G., & Hersen, P. (2015). Real-time control of a genetic toggle switch. *Who Am I Colloquium*, Deauville, France.

Grant writing

National Science Foundation grant 2032357
"Single-cell feedback, optogenetics, and deep learning to control gene expression in bacteria"

- Came up with complete concept for grant.
- Wrote entire draft of proposal.

- Worked with Dr. Dunlop on grantsmanship and refining project objectives.
- Responded to reviewer feedback.
- Grant was funded.

Department of Energy grant DE-SC0019387
"High-throughput chemical imaging for optimizing biofuel synthesis using synthetic biology"
- Wrote all of one objective (out of three).
- Generated preliminary data demonstrating feasability of project goals.
- Worked with collaborators and project PIs to develop proposal ideas.
- Grant was funded.

National Science Foundation grant 2143289
"Transitions: Deep Learning Models for Microbial Image Analysis and Time-Series Predictions"
&
National Institutes of Health grant R01AI102922
"Cell-to-cell heterogeneity and the emergence of antibiotic resistance"
- Provided feedback and input on early drafts.
- Both grants were funded.

Teaching *&* mentoring experience

- Guest lecturer in BE404 Control Theory, Boston University, Under-graduate and graduate level.
- Guest lecturer in BE403 Signal Processing, Boston University, Under-graduate and graduate level.
- Supervision of 2 Master's students theses on mathematical modelling of real-time control of a genetic toggle switch.
- Supervision of 2 Master's students projects on machine learning based image analysis of microscopy images.
- Co-supervision of a Master's student thesis on biological laboratory design and social interactions within a research group.
- Supervision of 5 PhD rotation projects, on a range of topics including CRISPR-based genomic integration, deep learning-based image processing, or synthetic circuit design.
- Supervision of 2 Senior design project teams, for the development of automated sample preparation devices, and for a cloud-computing based web interface for microscopy image analysis.
- Supervision of International Genetically Engineered Machine competition (iGEM) Grenoble team 2012, especially for mathematical modelling of gene expression.

Summary of qualifications *&* proficiencies

Technical skills

Deep model-predictive control • Reinforcement learning
Microbiology • Molecular biology • Optogenetics
Deterministic *&* stochastic modelling of genetic and metabolic networks
Computer vision • Deep learning
Microfabrication *&* microfluidics • Microscopy • Automation • Instrumentation

3D printing • Rapid prototyping • Electronics
Python • Matlab • C/C++ • Tensorflow & Pytorch • Git • Unix/Linux

Leadership & communication

10+ years of scientific project management, as part of a team, a larger collaboration, or as main researcher, from conception to publication and follow-up studies.

10+ years of scientific communication, by presenting at conferences and writing journal articles.

Collaboration on open-source and open data research projects and active support for the community, for example on a software for microscopy time-lapse analysis (DeLTA).

Co-organizer of the Biocontrol seminars, a series of monthly online seminars featuring international speakers.

References

Prof. Mary J. Dunlop — Boston University — Post-doctoral advisor — mjdunlop@bu.edu

Prof. Pascal Hersen — Cnrs & Curie Institute — PhD advisor — pascal.hersen@curie.fr

Prof. Grégory Batt — Inria & Pasteur Institute — PhD advisor — gregory.batt@inria.fr

Prof. Ji-Xin Cheng — Boston University — Post-doctoral collaborator — jxcheng@bu.edu

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