

Hugo Miguel Raposo Correia Botelho

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1749-016 Lisboa
Portugal



BIOGRAPHICAL NOTE

Scientist with a strong expertise in microscopy, high content screening, cell biology, biochemistry and biophysics. Cystic Fibrosis researcher. Manager of the High-Throughput Screening Facility from BioISI / Faculty of Sciences, University of Lisbon. Bioimage analyst, software developer, data scientist, trainer and academic supervisor.

MAIN SKILLS

Cystic Fibrosis	CFTR traffic and folding; Cystic Fibrosis cellular models; therapeutic target identification.
Management	Manager of High-Throughput Screening Facility (BioISI/FCUL); Project management.
Microscopy	High-content microscopy screening. Widefield and confocal fluorescence.
Bioimage analysis	Quantification and feature extraction from microscopy images (ImageJ, CellProfiler).
Cell Biology	Assay design; Eukaryotic and prokaryotic cell culture; RNA interference; Membrane trafficking.
Data Science	Statistical analysis of microscopy screening datasets. Data visualization, exploration and normalization.
Software development	R and ImageJ. Standalone scripts, libraries and web applications.
Training	Organization of courses and training sessions on microscopy, screening and image analysis.
Biochemistry	Protein expression, purification and characterization; Liquid chromatography; SDS-PAGE; Western blot; Proteomics.
Biophysics	Spectroscopy (UV-visible Absorption, Fluorescence Emission, Circular Dichroism, FT-IR, Dynamic Light Scattering); Protein folding, misfolding and aggregation; Thermodynamics; Protein aggregation; Electrochemistry.

EDUCATION

2010	PhD in Biochemistry. Specialization: Biophysics. ITQB / Universidade Nova de Lisboa. Approved by unanimity Supervisor: Cláudio M. Gomes <u>Thesis title:</u> Protein folding and metal ions – Conformational and functional interplay
2006	Degree in Biochemistry (Licenciatura, pre-Bologna). Faculty of Sciences, University of Lisboa. Mark: 18/20 Supervisor: Cláudio M. Gomes <u>Thesis title:</u> Pesquisa, identificação e caracterização de proteínas hiperestáveis no proteoma solúvel da archaea hipertermofílica <i>Sulphurisphaera</i> sp. [Search, identification and characterization of hyperstable proteins in the soluble proteome of the hyperthermophilic archaea <i>Sulphurisphaera</i> sp.]

SCIENTIFIC CAREER

- 2019, Jul - today **Facility Manager**, High-Throughput Screening Facility. BioISI, FCUL.
- 2019, Jul - today **Junior Researcher**, BioISI, FCUL.
Using high-content siRNA screening for the identification and characterization of CFTR regulator genes. Development of bioimage analysis software.
- 2012, Apr – 2019, Jun **Post-Doctoral Fellow**. BioISI, FCUL.
Identification and characterization of therapeutically relevant proteins rescuing CFTR traffic in Cystic Fibrosis using siRNA-based high-throughput microscopy screens. Development of automated image analysis pipelines and biostatistical analysis software. Supervisor: Margarida D. Amaral.
- 2012, Jul – 2013, Dec **Post-Doctoral Fellow**, Advanced Light Microscopy Facility, EMBL Heidelberg, Germany.
Training on high-throughput microscopy (). Screening of siRNA libraries to identify CFTR modulators. Supervisors: Rainer Pepperkok, Margarida D. Amaral.
- 2011, Sep – 2012, Apr **Post-Doctoral Fellow**, ITQB/UNL.
Biophysical characterization of amyloidogenesis in S100 proteins. Supervisor: Cláudio Gomes.
- 2011, Jul - Oct **Post-Doctoral Fellow**, Department of Neuropathology. Freiburg University, Germany.
Neuropathological analysis of S100 deposits in animal and cellular models of Alzheimer's disease. Crystallographic characterization of S100 amyloids. Supervisor: Günter Fritz.
- 2010, Nov - 2011, Jun **Post-Doctoral Fellow**, ITQB/UNL.
Characterization of the amyloidogenic propensity of S100 proteins in physiological-like conditions. Supervisor: Cláudio M. Gomes.
- 2010, Jan - Feb **Visiting PhD Student**, Umeå University, Sweden.
Cytotoxicity of S100 amyloids, Supervisor: Ludmilla Morozova-Roche.
- 2006 - 2010 **PhD Student**, ITQB/UNL.
Modulation of the conformation, stability and amyloidogenesis of S100 proteins by metal ions. Conformation and stability of iron-sulfur proteins. Supervisor: Cláudio M. Gomes.
- 2005 - 2006 **Undergraduate research student**, FCUL Biochemistry course. ITQB/UNL.
Proteome wide analysis of protein stability in the hyperthermophile *Sulphurisphaera sp.*, Supervisor: Cláudio M. Gomes.

PUBLICATIONS

h-index: 12

Online publication list and statistics:

<http://www.researcherid.com/rid/B-3092-2008>

<http://orcid.org/0000-0002-4208-1086>

https://www.researchgate.net/profile/Hugo_Botelho

<https://www.scopus.com/authid/detail.url?authorId=15030102200>

<http://www.ncbi.nlm.nih.gov/sites/myncbi/1X9J-JV7QTAQu/bibliographay/47769077/public>

<http://www.linkedin.com/pub/hugo-botelho/27/5b9/b60>

<http://scholar.google.com/citations?user=nXftyYwAAAAJ>

Papers in international peer reviewed journals

1. Hagemeyer MC, Vonk AM, Awatade NT, Silva IAL, Tischer C, Hilsenstein V, Beekman JM, Amaral MD, Botelho HM (2021) **An open-source high-content analysis workflow for CFTR function measurements using the forskolin-induced swelling assay.** *Bioinformatics*, 36(24): 5686-5694. DOI: [10.1093/bioinformatics/btaa1073](https://doi.org/10.1093/bioinformatics/btaa1073)

2. Silva IAL, Doušová T, Ramalho S, Centeio R, Clarke LA, Railean V, [Botelho HM](#), Holubová A, Valášková I, Yeh J-T, Hwang T-C, Farinha CM, Kunzelmann K, Amaral MD (2020) **Organoids as a Personalized Medicine Tool for Ultra-Rare Mutations in Cystic Fibrosis: the Case of S955P and 1717-2A>G**. *Biochim Biophys Acta – Mol Basis Dis*, 1866, 165905. DOI: [10.1016/j.bbadis.2020.165905](https://doi.org/10.1016/j.bbadis.2020.165905)
3. Uliyakina I, da Paula AC, Afonso S, Lobo MJ, Felício V, [Botelho HM](#), Farinha CM, Amaral MD (2020) **Full rescue of F508del-CFTR processing and function by CFTR modulators can be achieved by removal of two regulatory regions**. *Int J Mol Sci*, 21(12): 4524. DOI: [10.3390/ijms21124524](https://doi.org/10.3390/ijms21124524)
4. Santos JD, Canato S, Carvalho AS, [Botelho HM](#), Aloria K, Amaral MD, Matthiesen R, Falcão AO, Farinha CM (2019) **Folding status is determinant over traffic-competence in defining CFTR interactors in the endoplasmic reticulum**. *Cells*, 8(4): 353. DOI: [10.3390/cells8040353](https://doi.org/10.3390/cells8040353)
5. Palma E, [Botelho HM](#), Morais GR, Rodrigues I, Santos IC, Campello MPC, Raposinho P, Belchior A, Gomes SS, Araújo MF, Correia I, Ribeiro N, Gama S, Mendes F, Paulo A (2019) **Unravelling the antitumoral potential of novel bis(thiosemicarbazonato) Zn(II) complexes: structural and cellular studies**. *J Biol Inorg Chem*, 24: 71-89. DOI: [10.1007/s00775-018-1629-6](https://doi.org/10.1007/s00775-018-1629-6)
6. Awatade NT, Ramalho S, Silva IAL, Felício V, [Botelho HM](#), de Poel E, Vonk A, Beekman JM, Farinha CM, Amaral MD (2018) **R560S: a class II CFTR mutation that is not rescued by current modulators**. *J Cyst Fibros*, 18(2):182-189. DOI: [10.1016/j.jcf.2018.07.001](https://doi.org/10.1016/j.jcf.2018.07.001)
7. Cristóvão JS, Morris VK, Cardoso I, Leal SS, Martinez J, [Botelho HM](#), Göbl C, David R, Kierdorf K, Alemi M, Madl T, Fritz G, Reif B, Gomes CM (2018) **The neuronal S100B protein is a calcium-tuned suppressor of amyloid- β aggregation**. *Sci Adv*, 4(6): eaaq1702. DOI: [10.1126/sciadv.aaq1702](https://doi.org/10.1126/sciadv.aaq1702)
8. Lérias JR*, Pinto MC*, [Botelho HM](#), Awatade NT, Quaresma MC, Silva IAL, Wanitchakool P, Schreiber R, Pepperkok R, Kunzelmann K, Amaral MD (2018) **A novel microscopy-based assay identifies extended synaptotagmin-1 (ESYT1) as a positive regulator of anoctamin 1 traffic**. *Biochim Biophys Acta - Mol Cell Res*, 1865(2): 421-431. DOI: [10.1016/j.bbamcr.2017.11.009](https://doi.org/10.1016/j.bbamcr.2017.11.009)
9. Igreja S, Clarke LA, [Botelho HM](#), Marques L, Amaral MD (2015) **Correction of a cystic fibrosis splicing mutation by antisense oligonucleotides**. *Human mutat*, 37(2): 209-215. DOI: [10.1002/humu.22931](https://doi.org/10.1002/humu.22931)
10. Clarke LA, [Botelho HM](#), Sousa L, Falcão AO, Amaral MD (2015) **Transcriptome meta-analysis reveals common differential and global gene expression profiles in cystic fibrosis and other respiratory disorders and identifies CFTR regulators**. *Genomics*, 106(5): 268-277. DOI: [10.1016/j.ygeno.2015.07.005](https://doi.org/10.1016/j.ygeno.2015.07.005)
11. [Botelho HM](#), Uliyakina I, Awatade NT, Proença MC, Tischer C, Sirianant L, Kunzelmann K, Pepperkok R, Amaral MD (2015) **Protein traffic disorders: an effective high-throughput fluorescence microscopy pipeline for drug discovery**. *Sci Rep*, 5, 9038. DOI: [10.1038/srep09038](https://doi.org/10.1038/srep09038)
12. Carvalho SB, [Botelho HM](#), Leal SS, Cardoso I, Fritz G, Gomes CM (2013) **Intrinsically disordered and aggregation prone regions underlie β -aggregation in S100 proteins**. *PLoS ONE*, 8, e76629. DOI: [10.1371/journal.pone.0076629](https://doi.org/10.1371/journal.pone.0076629)
13. Sá-Moura B, Simões AM, Fernandes H, Fraga J, Abreu IA, [Botelho HM](#), Gomes CM, Marques AJ, Dohmen J, Ramos P, Macedo-Ribeiro S (2013) **Biochemical and biophysical characterization of recombinant yeast proteasome maturation factor ump1**. *Comput Struct Biotechnol J*, 7(8), e201304006. DOI: [10.5936/csbj.201304006](https://doi.org/10.5936/csbj.201304006)
14. [Botelho HM](#), Leal SS, Cardoso I, Yanamandra K, Morozova-Roche LA, Fritz G, Gomes CM (2012) **S100A6 amyloid fibril formation is calcium-modulated and enhances superoxide dismutase-1 (SOD1) aggregation**. *J Biol Chem*, 287(50): 42233-42. DOI: [10.1074/jbc.M112.396416](https://doi.org/10.1074/jbc.M112.396416)
15. Leal SS*, [Botelho HM](#) *, Gomes CM (2012) **Metal ions as modulators of protein conformation and misfolding in neurodegeneration**. *Coord Chem Rev*, 256: 2253-2270. (*equally contributing authors). DOI: [10.1016/j.ccr.2012.04.004](https://doi.org/10.1016/j.ccr.2012.04.004)
16. Veith A, [Botelho HM](#), Kindinger F, Gomes CM, Kletzin A (2012) **The sulfur oxygenase reductase from the mesophilic bacterium *Halothiobacillus neapolitanus* is a highly active thermozyyme**. *J Bacteriol*, 194: 677-685. DOI: [10.1128/JB.06531-11](https://doi.org/10.1128/JB.06531-11)

17. [Botelho HM](#), Gomes CM (2011) **Structural reorganization renders enhanced metalloprotein stability.** *Chem Commun*, 47: 11149-11151. DOI: [10.1039/c1cc13354c](https://doi.org/10.1039/c1cc13354c)
18. Fritz G, [Botelho HM](#), Morozova-Roche LA, Gomes CM (2010) **Natural and amyloid self-assembly of S100 proteins: structural basis of functional diversity.** *FEBS J*, 277: 4578-90. DOI: [10.1111/j.1742-4658.2010.07887.x](https://doi.org/10.1111/j.1742-4658.2010.07887.x)
19. [Botelho HM](#), Leal SS, Veith A, Prosinecki V, Bauer, C., Fröhlich, R., Kletzin A, Gomes CM (2010) **Role of a novel disulfide bridge within the all-beta fold of soluble Rieske proteins.** *J Biol Inorg Chem*, 15: 271-281. DOI: [10.1007/s00775-009-0596-3](https://doi.org/10.1007/s00775-009-0596-3)
20. [Botelho HM](#), Koch M, Fritz G, Gomes CM (2009) **Metal ions modulate the folding and stability of the tumor suppressor protein S100A2.** *FEBS J*, 276(6): 1776-86. DOI: [10.1111/j.1742-4658.2009.06912.x](https://doi.org/10.1111/j.1742-4658.2009.06912.x)
21. Prosinecki V, [Botelho HM](#), Francese S, Mastrobuoni G, Moneti G, Urich T, Kletzin A, Gomes CM (2006) **A proteomic approach toward the selection of proteins with enhanced intrinsic conformational stability.** *J Proteome Res*, 5(10): 2720-6. DOI: [10.1021/pr0602491](https://doi.org/10.1021/pr0602491)

Book Chapters

1. Amaral MD, Farinha CM, Matos P, [Botelho HM](#) (2016) **Investigating alternative transport of integral plasma membrane proteins from the ER to the Golgi: lessons from the cystic fibrosis transmembrane conductance regulator (CFTR),** *In* Unconventional Protein Secretion: Methods in Molecular Biology, vol. 1459 (Pompa, A., and De Marchis, F., Eds.) 105-126. Humana Press, New York. DOI: [10.1007/978-1-4939-3804-9_7](https://doi.org/10.1007/978-1-4939-3804-9_7)
2. Carvalho SB, Cardoso I, [Botelho HM](#), Yanamandra K, Fritz G, Gomes CM, Morozova-Roche LA (2014) **Structural heterogeneity and bioimaging of S100 amyloid assemblies,** *in* Bionanoimaging: Protein Misfolding and Aggregation (Uversky, V., Lyubchenko, Y., eds), 197-212. Academic Press, Boston. DOI: [10.1016/B978-0-12-394431-3.00018-3](https://doi.org/10.1016/B978-0-12-394431-3.00018-3)
3. [Botelho HM](#), Fritz G, Gomes CM (2012) **Analysis of S100 oligomers and amyloids,** *in* Amyloid Proteins: Methods and Protocols, Methods in Molecular Biology, vol. 849 (Sigurdsson E.M., Calero, M., Gasset, M., eds), 373-386. Springer Science+Business Media. DOI: [10.1007/978-1-61779-551-0_25](https://doi.org/10.1007/978-1-61779-551-0_25)

SERVICE AS EXPERT REVIEWER FOR SCIENTIFIC JOURNALS

Biochimie
FEBS Letters
Journal of Biotechnology
Journal of Dermatological Research
Metallomics
Molecular Genetics & Genomic Medicine
Physical Chemistry Chemical Physics
PLoS One
Scientific Reports
SLAS Discovery

Online reviewing statistics:
<http://publons.com/a/1484264>

SOFTWARE PORTFOLIO

<http://github.com/hmbotelho>

LECTURING ACTIVITY

2017-2021	Functional screens and high throughput microscopy in drug discovery. Lecture for FCUL Data Science Post Graduation. Omics approaches in biomedicine and biotechnology module (1/year). Course responsible: Margarida Gama-Carvalho.
2016-2021	Fluorescence Microscopy. Lecture for FCUL Biochemistry Master's course. Complements in Biochemical Analysis module (1/year). Course responsible: Cláudio M. Gomes or Ana Coutinho.
2021, Feb 4	High-throughput microscopy & Screening. Lecture at online course "Optical microscopy at Optical microscopy at COLife & Friends: learning the basics". [https://youtu.be/tGnOiOUk2j8]. Course organizer: COLife.
2020, Nov 24	Princípios e Aplicações da Microscopia de High-Throughput [Principles and Applications of High-Throughput Microscopy]. Lecture for ISEL's Graduation Course on Biomedical Engineering. Biology and Histology module. Course responsible: Rita Pacheco.
2020, Feb-Jun	Biochemistry, Laboratory lectures. Biology degree FCUL, 1 st year, 1 st semester.
2016-2020	High-throughput microscopy & screening. Lecture for FCUL Animal Biology Department Master's course. Bioimaging module (1/year). Course responsible: Gabriel Martins.
2019, Mar 27	CellProfiler & CellProfiler Analyst workshop. Practical demo for the micro-Workshop "Introduction to Image Processing and Analysis using Fiji". Instituto Gulbenkian de Ciência / Advanced Imaging Unit. Workshop organization: Nuno Pimpão Martins.
2018, Oct 24	Workshop on High Content Screening and Data Mining. Software demo. SPAOM2018: Spanish Portuguese Meeting for Advanced Optical Microscopy. Granada, Spain.
2018, Oct 18	Image analysis open source programs: ImageJ, CellProfiler and others. Training session on open source image analysis software. CNIO High Content Screening School. Madrid, Spain. Organizer: Diego Megias.
2017-2018	High content analysis of the forskolin Induced swelling assay. Lecture for BioISI PhD program & Hands-on workshop on Epithelial Systems: Physiology and Pathophysiology (1/year).
2014-2018	Introduction to High-Throughput Microscopy, Image acquisition, Data analysis in High-Throughput Microscopy, Assay development in High-Throughput Microscopy, High-Throughput Microscopy bioassay & Discussion of the experimental work [6 lectures/year]. Hands-on workshop on High-Throughput Microscopy. BioISI PhD Programme in Biology/Biochemistry (BioSYS).
2016-2018	Data analysis in high content microscopy screening. Course on High Throughput Screening and Image Analysis for Biosciences (1/year). I3S. Porto, Portugal. Organizer: André Maia.
2017, Apr 5&19	Scientific image editing workshop. Organizer: ipSC – commission of post-graduate students of the Faculty of Pharmacy of the University of Lisbon.
2017, Feb 12-15	Building a workflow with CellProfiler. Instructor in NEUBIAS BioImage Analysis Training School for Early Career Investigators. Oeiras, Portugal.
2013, Oct 23 - 24	High Content Screening in Cystic Fibrosis Biomedical Research. EMBL Predoc Course 2013. Cell Biology module. Practical sessions.

COORDINATION OF RESEARCH PROJECTS

2020	VALHealth – Valorisation of Algae for Health: Bioactive Compounds from Marine Bioresources by Membrane Technology BioISI Project. Principal Investigators: Rita Pacheco & Hugo M. Botelho .
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- 2018 **Deconvolution of dual CFTR/ANO1 Modulators from Portuguese natural products – A new class of drugs for CF therapy**
BioISI Project. Principal Investigators: Helena Gaspar, Helena Vieira & [Hugo M. Botelho](#).
- 2017 **A new class of drugs for CF therapy - Dual CFTR/ANO1 Modulators from Portuguese natural products**
BioISI Project. Principal Investigators: [Hugo M. Botelho](#) & Helena Vieira.
- 2016 **Natural compounds as a source of novel drug leads for Cystic Fibrosis**
BioISI Project. Principal Investigators: [Hugo M. Botelho](#) & Helena Vieira.
- 2016 **The identification of new natural compounds of high therapeutic potential for Cystic Fibrosis by high-throughput microscopy screens**
BioISI Post-Doc. Supervisors: [Hugo M. Botelho](#) & Helena Vieira.
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ORGANIZATION OF SCIENTIFIC MEETINGS

- 2021 **SPAOM2021 – Spanish-Portuguese Advanced Optical Microscopy 2021**
Member of the scientific committee & HCS Community Workshop Organizer
23-25 November, Online
<https://igc.idloom.events/spaom2021>
- 2021 **Eutopia 3 – Third Meeting of the European Topology Interdisciplinary Initiative**
Member of the local organizing committee
15-17 February, Faculty of Sciences, University of Lisbon
<http://eutopia3.campus.ciencias.ulisboa.pt>
- 2019 **Workshop on Integrative Approaches to Protein Folding & Aggregation**
Organizing Committee
11-12 June, Faculty of Sciences, University of Lisbon
<http://folding2019.campus.ciencias.ulisboa.p/>
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ORGANIZATION OF TRAINING EVENTS

- 2021 **Basics in Light Microscopy**
25-28 October. Online.
Participants: 38
<https://fculmf.campus.ciencias.ulisboa.pt/blm2021>
- 2021 **Introduction to Image Analysis COLife & FCUL**
21-23 September. Online.
Participants: 218
- 2018 **Hands-on Workshop on High-Throughput Microscopy**
9-13 July. BioISI/FCUL. Lisbon, Portugal.
Participants: 17
<https://fculmf.campus.ciencias.ulisboa.pt/htm2018>
- 2017 **Hands-on Workshop on High-Throughput Microscopy**
17-21 July. BioISI/FCUL. Lisbon, Portugal.
Participants: 21
<https://fculmf.campus.ciencias.ulisboa.pt/htm2017>
- 2016 **Hands-on Workshop on High-Throughput Microscopy**
11-15 July. BioISI/FCUL. Lisbon, Portugal.
Participants: 11
- 2015 **Hands-on Workshop on High-Throughput Microscopy**
18-20 March. BioISI/FCUL. Lisbon, Portugal.
Participants: 11

PUBLIC AWARENESS OF SCIENCE ACTIVITIES

1. Ciências Research Day – Open Labs. **BioISI High-Throughput Screening Facility** Oct 27. Lisboa, Portugal.
2. FIC.A - Festival Internacional de Ciência. **A microscopia e a descoberta de novos fármacos** Oct 14. Oeiras, Portugal.
3. Dia Aberto Virtual FCUL. **Unidade de Microscopia** (2021) May 5. Online. https://www.youtube.com/playlist?list=PLlamaT8XLnu2_2X9gXVIUeggezhhNTohx

SCIENTIFIC SOCIETIES

2016-present NEUBIAS: Network of European BioImage Analysts, COST Action CA15124
2006 - present Portuguese Biochemical Society & Portuguese Biophysical Society

LANGUAGE SKILLS

Portuguese Native speaker.
English Excellent speaking, reading and writing.
French Basic speaking, reading and writing.
Spanish Basic speaking, reading and writing.

OTHER ACTIVITIES

2019-present Contact person of BioISI in **PPBI - Portuguese Platform of Bioimaging**.
2019-present Member of the **Lisbon Area Bioimaging Group (Lx-BIG)**.
2019-present Contact person of BioISI in the **PT-OPENSREEN** research infrastructure.
2016-present Member of **NEUBIAS**: Network of European BioImage Analysts, COST Action CA15124
2014 - present Collaborates in the **management of microscopy resources**. BioISI & Functional Genomics and Proteostasis Group (group leader: Margarida D. Amaral). BioISI/FCUL. Lisbon, Portugal.
2013 **Volunteer to the 36th European Cystic Fibrosis Society Conference**. Jun 12-15. Lisbon Congress Centre. Lisbon, Portugal.