

Hugo Miguel Raposo Correia Botelho

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University of Lisboa, Faculty of Sciences
BioISI - Biosystems & Integrative Sciences Institute

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BIOGRAPHICAL NOTE

I am a scientist with a strong expertise in microscopy, cell biology and protein folding *in vivo* and *in vitro*. In 2010 I obtained a PhD in biochemistry (specialty: biophysics) for studies on the folding and aggregation properties of bacterial, archaeal and human proteins under the supervision of Dr. Cláudio M. Gomes (ITQB/UNL).

In 2012 I joined Margarida D. Amaral's lab at FCUL to research novel therapeutics for the genetic misfolding disease Cystic Fibrosis (CF). For 1.5 years I was trained on high-throughput microscopy, RNA interference screening and membrane trafficking at EMBL Heidelberg under the supervision of Dr. Rainer Pepperkok. Since 2014 Currently I have been employing siRNA-based screens to identify and characterize novel therapeutic target genes for the most common CF mutation.

Over the last 7 years I have contributed to establishing a high throughput microscopy facility at BioISI/University of Lisboa, and now serve as its manager. Each year the facility provides 5000 hours of equipment access time to about 40 users regarding sample preparation, imaging and data analysis. I am engaged in developing and deploying automated image analysis algorithms for high content microscopy, software development and data science approaches to biological data.

I have authored 19 original peer reviewed publications in international scientific journals, 3 book chapters, have supervised students and post-docs and have been involved in several scientific research projects, both as team member and PI. As manager of BioISI's high throughput microscopy facility I represent my institution at several microscopy-related consortia and initiatives. I am also a regular trainer and speaker at microscopy and cystic fibrosis meetings and courses.

MAIN SKILLS

Cystic Fibrosis	CFTR traffic and folding; Cystic Fibrosis cellular models; therapeutic target identification.
Microscopy	High-throughput microscopy screening assays; Automated microscopy image analysis and quantification (fluorescence & brightfield); High content analysis (ImageJ, CellProfiler).
Cell Biology	Assay design; Eukaryotic and prokaryotic cell culture; RNA interference; Membrane trafficking.
Data Science	Development of statistical analysis software suitable for large datasets.
Software development	R and Python, including standalone and web applications.
Web design	WordPress in the optics of the user and HTML5 (basic).
Biochemistry	Protein expression, purification and characterization; Liquid chromatography; SDS-PAGE; Western blot; Proteomics.
Biophysics	Spectroscopy (UV-visible Absorption, Fluorescence, Circular Dichroism, FT-IR, Dynamic Light Scattering); Protein folding, misfolding and aggregation; Thermodynamics; Electrochemistry.
Management	Lab work supervision; Project management; Establishment of a microscopy facility: design and implementation of workspaces, IT infrastructure and work pipelines.

ACADEMIC PATHWAY

2010	PhD in Biochemistry. Specialization: Biophysics. ITQB/UNL. Approved by unanimity
2006	Degree in Biochemistry. FCUL. Pre-Bologna. Mark: 18/20

SCIENTIFIC ACTIVITY

2019, Jul - today	Junior Researcher. Functional Genomics and Proteostasis Group. BioISI, FCUL.
2012, Apr – 2019, Jun	Post-Doctoral Fellow. Functional Genomics and Proteostasis Group. BioISI, FCUL (Margarida D. Amaral)
2012, Jul – 2013, Dec	Post-Doctoral Fellow. EMBL, Heidelberg. (Rainer Pepperkok and Margarida D. Amaral)
2011, Sep – 2012, Apr	Post-Doctoral Fellow. Protein Biochemistry, Folding and Stability Group. ITQB/UNL (Cláudio M. Gomes)
2011, Jul - Oct	Post-Doctoral Fellow. Protein Biophysics and Biochemistry Group. Department of Neuropathology. Freiburg University, Germany (Günter Fritz).
2010, Nov - 2011, Jun	Post-Doctoral Fellow. Protein Biochemistry, Folding and Stability Group. ITQB/UNL (Cláudio M. Gomes).
2010, Jan - Feb	Visiting PhD Student. Department of Medical Biochemistry and Biophysics. Umeå University, Sweden (Ludmilla Morozova-Roche).
2006 - 2010	PhD Student. Protein Biochemistry, Folding and Stability Group. ITQB/UNL (Cláudio M. Gomes).
2005 - 2006	Undergraduate research student. FCUL Biochemistry course. Protein Biochemistry, Folding and Stability Group. ITQB/UNL (Cláudio M. Gomes).

ORGANIZATION OF SCIENTIFIC MEETINGS

2019	Workshop on Integrative Approaches to Protein Folding & Aggregation 11-12 June 2019. FCUL Organizing Committee: Hugo M. Botelho , Bárbara J. Henriques, Patrícia F.N. Faisca
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LECTURING ACTIVITY

2020, Feb-Jun	Biochemistry Laboratory lectures. Biology degree, 1 st year. Faculty of Sciences, University of Lisbon.
2020, Feb 19	High-throughput microscopy & screening. Lecture for FCUL's Animal Biology Department Master's course. Bioimaging module. Course responsible: Gabriel Martins.
2019, Dez 16	Screens funcionais e microscopia de larga escala na descoberta de novos fármacos [<i>Functional screens and high throughput microscopy indrug discovery</i>]. Lecture for FCUL's Data Science Post Graduation. Abordagens Ómicas em Biomedicina e Biotecnologia [<i>Omics approaches in biomedicine and biotechnology module</i>]. Course responsible: Margarida Gama-Carvalho.
2019, Oct 22	Microscopia de fluorescência [<i>Fluorescence Microscopy</i>]. Lecture for FCUL's Biochemistry Master's course. Complements in Biochemical Analysis module. Course responsible: Ana Coutinho.

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.
2019, Feb 20	High-throughput microscopy & screening. Lecture for FCUL's Animal Biology Department Master's course. Bioimaging module. Course responsible: Gabriel Martins.
2018, Dez 17	<i>Functional screens and high throughput microscopy indrug discovery.</i> Lecture for FCUL's Data Science Post Graduation. <i>Omics approaches in biomedicine and biotechnology module.</i> Course responsible: Margarida Gama-Carvalho.
2018, Oct 24	Workshop on High Content Screening and Data Mining. 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's High Content Screening School. Madrid, Spain.
2018, Oct 16	Microscopia de fluorescência [<i>Fluorescence Microscopy</i>]. Lecture for FCUL's Biochemistry Master's course. Complements in Biochemical Analysis module. Course responsible: Ana Coutinho.
2018, Jul 27	High content analysis of the forskolin Induced swelling assay. Lecture for BioISI's PhD program & Hands-on workshop. Epithelial Systems: Physiology and Pathophysiology. Lisbon, Portugal.
2018, Jul 9-13	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. Hands-on workshop on High-Throughput Microscopy. BioISI PhD Programme in Biology/Biochemistry (BioSYS). Lisbon, Portugal.
2018, Jun 22	Data analysis in high content microscopy screening. Course on High Throughput Screening and Image Analysis for Biosciences. I3S. Porto, Portugal.
2018, Jun 14	Introduction to Microscopy. Lecture for BioISI's PhD program. Functional genomics & Advanced light microscopy module. Lisbon, Portugal.
2018, Feb 22	High-throughput microscopy & screening. Lecture for FCUL's Animal Biology Department Master's course. Bioimaging module. Course responsible: Gabriel Martins.
2017, Dec 18	Screens funcionais e microscopia de larga escala na descoberta de novos fármacos [<i>Functional screens and high throughput microscopy indrug discovery</i>]. Lecture for FCUL's Data Science Post Graduation. Abordagens Ómicas em Biomedicina e Biotecnologia [<i>Omics approaches in biomedicine and biotechnology module</i>]. Course responsible: Margarida Gama-Carvalho.
2017, Oct 24	Microscopia de fluorescência [<i>Fluorescence Microscopy</i>]. Lecture for FCUL's Biochemistry Master's course. Complements in Biochemical Analysis module. Course responsible: Ana Coutinho.
2017, Jul 28	High content analysis of the forskolin Induced swelling assay. Lecture for BioISI's PhD program & Hands-on workshop. Epithelial Systems: Physiology and Pathophysiology. Lisbon, Portugal.
2017, Jul 17-21	Introduction to ImageJ, High-Throughput Microscopy bioassay, Image acquisition, Data analysis in High-Throughput Microscopy & Assay development in High-Throughput Microscopy. Hands-on workshop on High-Throughput Microscopy. BioISI PhD Programme in Biology/Biochemistry (BioSYS). Lisbon, Portugal.

2017, Jun 7	Data analysis in high content microscopy screening. 3 rd Course on High Content Screening and Image Analysis for Biosciences. I3S. Porto, Portugal.
2017, Apr 5 & 19	Scientific image editing workshop. Faculty of Pharmacy, University of Lisbon. Organizer: ipSC – commission of post-graduate students of the faculty of pharmacy of the University of Lisbon.
2017, Feb 21	High-throughput microscopy & screening. Lecture for FCUL's Animal Biology Department Master's course. Bioimaging module. Course responsible: Gabriel Martins.
2017, Feb 12-15	Building a workflow with CellProfiler. Instructor in NEUBIAS BioImage Analysis Training School for Early Career Investigators. Oeiras, Portugal.
2016, Nov 15	Microscopia de fluorescência [Fluorescence Microscopy]. Lecture for FCUL's Biochemistry Master's course. Course responsible: Cláudio M. Gomes.
2016, Jul 11-15	Introduction to ImageJ, High-Throughput Microscopy image acquisition & Assay development in High-Throughput Microscopy Hands-on workshop on High-Throughput Microscopy & BioISI PhD Programme in Biology/Biochemistry (BioSYS). Lisbon, Portugal.
2016, Jun 17	Data analysis and management in high content microscopy screening. 2 nd Course on High Content Screening and Image Analysis for Biosciences. I3S. Porto, Portugal.
2016, Feb 17	High-throughput microscopy & screening. Lecture for FCUL's Animal Biology Department Master's course. Bioimaging module. Course responsible: Gabriel Martins.
2015, Mar 16-20	High throughput screening: siRNA transfection, immunofluorescence and automated imaging of CFTR expressing cells. BioISI PhD Programme in Biology/Biochemistry (BioSYS). Laboratory classes.
2014, Apr 7 - 9	High throughput screening: siRNA transfection, immunofluorescence and automated imaging of CFTR expressing cells. BioFIG PhD Programme in Biology/Biochemistry (BioSYS). Laboratory classes.
2013, Oct 23 - 24	High Content Screening in Cystic Fibrosis Biomedical Research. EMBL Predoc Course 2013. Cell Biology module. Practical sessions.

COORDINATION OF SCIENTIFIC PROJECTS

2020	VALHealth – Valorisation of Algae for Health: Bioactive Compounds from Marine Bioresources by Membrane Technology. BioISI Project. 10,000€ Principal Investigators: Rita Pacheco & Hugo M. Botelho.
2018	Deconvolution of dual CFTR/ANO1 Modulators from Portuguese natural products – A new class of drugs for CF therapy. BioISI Project. 10,000€ 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. 10,000€ Principal Investigators: Hugo M. Botelho & Helena Vieira.
2016	Natural compounds as a source of novel drug leads for Cystic Fibrosis. BioISI Project. 10,000€ Principal Investigators: Hugo M. Botelho & Helena Vieira.

SERVICE AS EXPERT REVIEWER

Biochimie
FEBS Letters
Journal of Biotechnology
Journal of Dermatological Research
Metallomics
Physical Chemistry Chemical Physics
PLOS One
Scientific Reports
SLAS Discovery

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

PUBLICATIONS

h-index: 9

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>

Theses

1. Botelho, H.M. (2010) PROTEIN FOLDING AND METAL IONS – CONFORMATIONAL AND FUNCTIONAL INTERPLAY. Biochemistry PhD Thesis, ITQB/UNL.
2. Botelho, H.M. (2006) PESQUISA, IDENTIFICAÇÃO E CARACTERIZAÇÃO DE PROTEÍNAS HIPERESTÁVEIS NO PROTEOMA SOLÚVEL DA ARCHAEA HIPERTERMOFÍLICA *Sulfurisphaera sp.*. Biochemistry Degree Thesis, FCUL.

Papers in international peer reviewed journals

1. Uliyakina I., da Paula A.C., Afonso S., Lobo M.J., Felício V., Botelho H.M., Farinha C. M., Amaral, M.D. (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* *In press*
2. Santos J.D., Canato S., Carvalho A.S., Botelho H.M., Aloria K., Amaral M.D., Matthiesen R., Falcão A.O., Farinha C.M. (2019) FOLDING STATUS IS DETERMINANT OVER TRAFFIC-COMPETENCE IN DEFINING CFTR INTERACTORS IN THE ENDOPLASMIC RETICULUM. *Cells* 8(4): 353.
3. Palma E., Botelho H.M., Morais G.R., Rodrigues I., Santos I.C., Campello M.P.C., Raposinho P., Belchior A., Gomes S.S., Araújo M.F., 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.
4. Awatade N.T., Ramalho S., Silva I.A.L., Felício V., Botelho H.M., de Poel E., Vonk A., Beekman J.M., Farinha C.M., Amaral M.D. (2018) R560S: A CLASS II CFTR MUTATION THAT IS NOT RESCUED BY CURRENT MODULATORS. *J Cyst Fibros* 18(2):182-189.

5. Cristóvão J.S., Morris V.K., Cardoso I., Leal S.S., Martinez J., Botelho H.M., Göbl C., David R., Kierdorf K., Alemi M., Madl T., Fritz G., Reif B., Gomes C.M. (2018) THE NEURONAL S100B PROTEIN IS A CALCIUM-TUNED SUPPRESSOR OF AMYLOID-BETA AGGREGATION. **Sci Adv** 4(6): eaaq1702.
6. Lérias J.R.* , Pinto M.C.* , Botelho H.M., Awatade N.T., Quaresma M.C., Silva I.A.L., Wanitchakool P., Schreiber R., Pepperkok R., Kunzelmann K., Amaral M.D. (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.
7. Igreja, S., Clarke, L.A., Botelho, H.M., Marques, L., Amaral, M.D. (2015) CORRECTION OF A CYSTIC FIBROSIS SPLICING MUTATION BY ANTISENSE OLIGONUCLEOTIDES. **Human mutat**, 37(2): 209-215.
8. Clarke, L.A., Botelho, H.M., Sousa, L., Falcão, A.O., Amaral, M.D. (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.
9. Botelho H.M., Uliyakina, I, Awatade, N.T., Proença, M.C., Tischer, C., Sirianant, L., Kunzelmann, K., Pepperkok, R., Amaral, M.D. (2015) PROTEIN TRAFFIC DISORDERS: AN EFFECTIVE HIGH-THROUGHPUT FLUORESCENCE MICROSCOPY PIPELINE FOR DRUG DISCOVERY. **Sci Rep**, 5, 9038.
10. Carvalho, S.B., Botelho, H.M., Leal, S.S., Cardoso, I., Fritz, G., Gomes, C.M. (2013) INTRINSICALLY DISORDERED AND AGGREGATION PRONE REGIONS UNDERLIE β -AGGREGATION IN S100 PROTEINS. **PLoS ONE**, 8, e76629.
11. Sá-Moura, B., Simões, A.M., Fernandes, H., Fraga, J., Abreu, I.A., Botelho, H.M., Gomes, C.M., Marques, A.J., 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.
12. Botelho, H.M., Leal, S. S., Cardoso, I., Yanamandra, K., Morozova-Roche, L. A., Fritz, G., Gomes, C.M. (2012) S100A6 AMYLOID FIBRIL FORMATION IS CALCIUM-MODULATED AND ENHANCES SUPEROXIDE DISMUTASE-1 (SOD1) AGGREGATION. **J Biol Chem**, 287(50): 42233-42.
13. Leal, S.S.* , Botelho, H.M.* , Gomes, C.M. (2012) METAL IONS AS MODULATORS OF PROTEIN CONFORMATION AND MISFOLDING IN NEURODEGENERATION. **Coord Chem Rev**, 256: 2253-2270. (*equally contributing authors).
14. Veith, A., Botelho, H.M., Kindinger, F., Gomes, C.M., Kletzin, A. (2012) THE SULFUR OXYGENASE REDUCTASE FROM THE MESOPHILIC BACTERIUM *Halothiobacillus Neapolitanus* IS A HIGHLY ACTIVE THERMOZYME. **J Bacteriol**, 194: 677-685.
15. Botelho, H.M., Gomes, C.M., (2011) STRUCTURAL REORGANIZATION RENDERS ENHANCED METALLOPROTEIN STABILITY. **Chem Commun**, 47: 11149-11151.
16. Fritz, G., Botelho, H.M., Morozova-Roche, L.A., Gomes, C.M., (2010) NATURAL AND AMYLOID SELF-ASSEMBLY OF S100 PROTEINS: STRUCTURAL BASIS OF FUNCTIONAL DIVERSITY. **FEBS J**, 277: 4578-90.
17. Botelho, H.M., Leal, S.S., Veith, A., Prosinecki, V., Bauer, C., Fröhlich, R., Kletzin, A., Gomes, C.M. (2010) ROLE OF A NOVEL DISULFIDE BRIDGE WITHIN THE ALL-BETA FOLD OF SOLUBLE RIESKE PROTEINS. **J Biol Inorg Chem**, 15: 271-281.
18. Botelho, H.M., Koch, M., Fritz, G., Gomes, C.M. (2009) METAL IONS MODULATE THE FOLDING AND STABILITY OF THE TUMOR SUPPRESSOR PROTEIN S100A2. **FEBS J**, 276(6): 1776-86.
19. Prosinecki, V., Botelho, H.M., Francese, S., Mastrobuoni, G., Moneti, G., Urich, T., Kletzin, A. ,Gomes, C.M. (2006) A PROTEOMIC APPROACH TOWARD THE SELECTION OF PROTEINS WITH ENHANCED INTRINSIC CONFORMATIONAL STABILITY. **J Proteome Res**, 5(10): 2720-6.

Book Chapters

1. Amaral M.D., Farinha C.M., Matos P., Botelho H.M. (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.

2. Carvalho, S.B., Cardoso, I., Botelho, H.M., Yanamandra, K., Fritz, G., Gomes, C.M., Morozova-Roche, L.A. (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.
3. Botelho, H.M., Fritz, G., Gomes, C.M. (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.

Software portfolio

<http://github.com/hmbotelho>

SCIENTIFIC SOCIETIES

2016-present	NEUBIAS: Network of European BioImage Analysts, COST Action CA15124 (part of WG2 - training)
2006 - present	Portuguese Biochemical Society
2006 - present	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-OPENSOURCE infrastructure.
2018	Organizer of the "Hands-on Workshop on High-Throughput Microscopy". July 9 th -13 th . BioISI/FCUL. Lisbon, Portugal.
2017	Organizer of the "Hands-on Workshop on High-Throughput Microscopy". July 17 th -21 st . BioISI/FCUL. Lisbon, Portugal.
2016	Collaborated in the organization of "Hands-on Workshop on High-Throughput Microscopy". July 11 th -15 th . BioISI/FCUL. Lisbon, Portugal.
2015	Collaborated in the organization of "Hands-on Workshop on High-Throughput Microscopy". March 18 th -20 th . BioISI/FCUL. Lisbon, Portugal.
2014 - present	Collaborates in the management of microscopy resources. BioISI & Functional Genomics and Proteostasis Group (group leader: Margarida D. Amaral). BioISI/FCUL. Lisbon, Portugal.