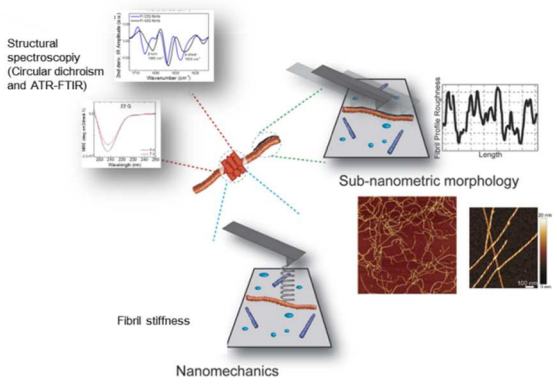
Proposta de Tema para Dissertação de Mestrado em Química (2018-2019)

Título	Nanoscopic characterization of the morphology of amyloid cores from pathological proteins involved in neurodegenerative diseases
Resumo	The formation of protein aggregates is a striking feature in multiple neurodegenerative diseases such as Alzheimer's Disease (AD). In these cases, a misfolded protein undergoes self-assembly resulting in the formation of highly organized protein fibrils called amyloid. What makes a protein fibrillate into amyloids in cells is still unclear, but we do know that amyloid protein aggregation is promoted by stacking of protein segments called Aggregation Prone Regions (APR). APR segments are short (up to 10 residues) have high hydrophobicity, low net charge and a high tendency to form β-structures. Naturally, different proteins have different APR segments within their primary sequence which generate highly polymorphic pre-fibrillar cores. An open question in the field relates to establishing the structures of such initial amyloid cores, as this would allow to gain insight not only into the basic molecular processes underlying the formation of fibrils but would also allow to design better anti-amyloid drugs that could be helpful in disease states. In this exciting project, we propose to characterize the morphologies of a diversity of such small amyloid cores through the analysis of a library of +50 chemically synthesized APR which have been designed from pathological proteins involved in neurodegenerative diseases and which we have demonstrated to be highly amyloidogenic. The project will develop with two aims: 1) to carry out a systematic nanoscopic analysis of the morphologies of each APR amyloid cores using high-resolution atomic force microscopy and associated methodologies; 2) to generate a library of structures of these amyloid core polymorphs to be organized into families according to scores from aggregation prediction algorithms such as TANGO and WALTZ; 3) to use advanced spectroscopic methods (Circular dichroism and ATR-FTIR) in selected peptides to obtain protein structural data.  This is a multidisciplinary project involving teams from different backgrounds – biochemistry and physics - which have been intensively collaborating during the last 2 years in the context of BioISI, to which both laboratories are affiliated. Therefore we are open to consider highly motivated candidates keen to advanced instrumental analysis, able to work independently and with an excellent academic record from a relevant background (chemistry, physics, biochemistry). The candidate will benefit from this unique research setting and will gain experience in handling and preparation of peptide solutions and learn to operate an AFM in dynamic model.
Local de trabalho	FCUL – Protein folding and misfolding laboratory (DQB) and Bio-PhysNano – BioPhysics and Nanosystems Group (DF)
Orientador (es)	Prof. Cláudio M. Gomes (DQB) and Dr. Mário S. Rodrigues (DF)
Informações	If you are interested e-mail cmgomes@fc.ul.pt attaching a brief cv including your academic record. More at http://folding.fc.ul.pt/ and http://bioisi.pt/biophysnano/