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**Center for Paralysis Research Special Seminar**

**Friday, April 19, 2024**

**1:30-2:30 PM in DLR 131**

**Biological shapes emerging from physics at the nanoscale**

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*Abstract:* We usually consent, consciously or not, to the restriction of looking at biological systems through disciplinary lenses. In our siloed ecosystem, biochemists, geneticists, molecular cell biologists, neuroscientists, statisticians, etc. focus on the processes involving the digital parts (genes, proteins, molecules, action potentials, networks, systems, -omics), while physicists, applied mathematicians and engineers often centre on biological analogue behaviour (e.g. mechanics, bioelectricity). Yet, despite its successes, the disciplinary approach to biology has limitations: important biological and medical problems cannot be solved within disciplinary silos. And, from a purely scientific perspective, the narrow disciplinary lens produces in some of us a deep unease: unlike compartmentalised science, biology emerged on Earth precisely from the dynamic coupling of biochemical and physical properties, digital and analogue. To “know” biology we must face the “coupling problem”, or as engineers put it “the multiphysics of biology”.

In my talk, I will propose that the key to understand the integration of properties within biological shapes is to investigate them using the framework of “thermodynamics” and will discuss our attempts to use the atomic force microscope (AFM) to understand how that might be achieved. I will reflect on how the shapes of biological cells, tissues and organisms emerge from a complex interplay of physics, biochemistry and genetics (evolution) by dissipating mechanical energy so they create time responses at different spatial scales that characterise the way they alter/grow/connect their shapes as they interact with their environment. Measuring viscoelasticity (i.e. mechanical/thermodynamic time) at the nanoscale in living systems remains experimentally challenging [1,2]. I will present AFM-based techniques to map the viscoelasticity of living tissues, cells, membranes, collagen, extracellular matrices, and tissue engineering matrices across the spatial and temporal scales, and chirp-based nanospectroscopic techniques [3] developed in my lab. Our results have uncovered that extracellular matrices of both living plants and tumours present an almost perfect linear viscoelastic behaviour that is key to understand their growth and shape. I will present our work showing how the growth and shape of the roots, leaves and hypocotyl of living Arabidopsis thaliana living plants are related to the nanoscale viscoelasticity of plant cell walls [4] and how this can be understood using concepts and theories from non-equilibrium thermodynamics, based on Onsager’s variational principle. I will also show how this knowledge can be used to understand how neurons need to couple electrophysiology and mechanics [5] and finally how we can use this knowledge to create “smart” bioinspired, low energy materials/computers , which will progressively harness biological properties, such as adaptation, and eventually learning/processing information [6].

[1] “Multifrequency AFM reveals lipid membrane mechanical properties and the effect of cholesterol in modulating viscoelasticity” 2019. Z Al-Rekabi, S Contera; Proceedings of the National Academy of Sciences 115 (11), 2658-2663.
[2] “Mapping nanomechanical properties of live cells using multi-harmonic atomic force microscopy” 2011 A Raman, S Trigueros, A Cartagena, APZ Stevenson, M Susilo, E Nauman, S Contera. Nature Nanotechnology 6 (12), 809.
[3] “Nanoscale Rheology: Dynamic Mechanical Analysis over a Broad and Continuous Frequency Range Using Photothermal Actuation Atomic Force Microscopy” 2024 A. R. Piacenti, C. Adam, N. Hawkins, R. Wagner, J. Seifert, Y. Taniguchi, R. Proksch, and S. Contera. ACS Macromolecules, in press https: //doi.org/10.1021/acs.macromol.3c02052.
[4] “Mapping cellular nanoscale viscoelasticity and relaxation times relevant to growth of living Arabidopsis thaliana plants using multifrequency AFM”2021 J Seifert, C Kirchhelle, I Moore, S Contera. Acta Biomaterialia;121:371-382.
[5] “Action of the general anaesthetic isoflurane reveals coupling between viscoelasticity and electrophysiological activity in individual neurons” 2023 C. Adam, C. Kayal, A. Ercole, S. Contera, H. Ye & A. Jerusalem Communications Physics 6: 174 & “Electrophysiological-mechanical coupling in the neuronal membrane and its role in ultrasound neuromodulation and general anaesthesia” 2019A Jerusalem…S Contera Acta Biomater. Oct 1:97:116-140.
[6] “Nano comes to life: How nanotechnology is transforming medicine and the future of biology” Sonia Contera, Princeton University Press 2019 & “Nanotecnología viva” Arpa Editores 2023.