## Probing cell volume in compressed tissues with Brillouin light scattering

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Volume regulation is key in maintaining important tissue functions, such as growth or healing [1]. This is achieved by modulation of active contractility, as well as water efflux that change molecular crowding within individual cells. Local sensors have been developed to monitor stresses or forces in model tissues, but these approaches do not capture the contribution of liquid flows to volume regulation. Here we use a new tool based on Brillouin light scattering (BLS) that uses the interaction of a laser light with inherent picosecond timescale density fluctuations in the sample [2]. To investigate volume variations, we induced osmotic perturbations with a polysaccharide osmolyte, Dextran (Dx), and compress multicellular spheroids (MCS). During osmotic compressions we observe an increase in the BLS frequency shift that reflects local variations in the refractive index and compressibility. Comparison of local cell compressions within the tissue with small Dx to macroscopic compressions with large Dx reveals the dominant contribution of cell volume to BLS response. To elucidate these data, we propose a model based on a mixing law that describes the increase of molecular crowding upon reduction of the intracellular fluids. Comparison with the data suggests a non-linear increase of the compressibility due to the dense crowding that induces hydrodynamic interactions between the cellular polymers.

[1] Cadart, et al. Nat. Phys. 15, 993-1004 (2019)

[2] Scarcelli, et al. Nat. Methods 12, 1132-1134 (2015).