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Structure and function of Ca^{2+} signalling pathways

My lab aims to understand how spatially organized intracellular Ca^{2+} signals are generated and decoded. We apply a range of approaches, which include single-molecule optical and electrophysiological analyses, to address the workings of intracellular Ca^{2+} channels, notably IP_3 receptors and ryanodine receptors in the endoplasmic reticulum, and two-pore channels in lysosomes [1]. At the structural level we are asking, with atomic resolution structures, how IP_3 and Ca^{2+} binding cause the pore of the IP_3 receptor to open [2, 3]. Within intact cells, we need to understand how interactions between different Ca^{2+} channels in mobile intracellular organelles interact to produce spatially organized Ca^{2+} signals [4]. Finally, we are concerned with understanding how information from different G protein-coupled receptors passes through the cell to regulate Ca^{2+} signals [5, 6].

Ca^{2+} signalling in osteocytes

Osteocytes are the most abundant cells in bone. Trapped within the bone matrix, they coordinate bone remodelling by regulating the activities of osteoblasts and osteoclasts in response to mechanical signals and chemical messengers [7]. They also secrete hormones that regulate more distant tissues. Ageing, inflammatory diseases and some drug treatments can lead to death of osteocytes or their dysfunction causing such diseases as osteoporosis. Very little is known of how changes in cytosolic Ca^{2+} concentration regulate osteocyte behaviour. This project will use single-cell imaging of cultured osteocytes (MLO-Y4 cells) to examine the effects of known regulators of osteocyte behaviour on cytosolic Ca^{2+} signals.

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