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## The store-operated calcium entry signal plex

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**Introduction:** Agonist-induced depletion of the intracellular Ca<sup>2+</sup> stores leads to the initiation of a signaling cascade that results in the opening of plasma membrane Ca<sup>2+</sup>-permeable channels. The so-called store-operated Ca<sup>2+</sup> entry (SOCE) is a major mechanism for Ca<sup>2+</sup> influx regulated by the filling state of the agonist-sensitive Ca<sup>2+</sup> pools. Ca<sup>2+</sup> influx via SOCE is required for the maintenance of sustained elevations in cytosolic Ca<sup>2+</sup> concentrations, required for the full activation of a number of physiological events, and to refill the intracellular stores. The mechanism underlying the communication of the filling state of the Ca<sup>2+</sup> stores to the plasma membrane channels, as well as the nature of the channels have been a matter of intense research in the last three decades. STIM1, an EF-hand containing protein located in the membrane of the endoplasmic reticulum and other agonist-sensitive stores, as well as the plasma membrane, has been reported to communicate the information of the filling state of the Ca<sup>2+</sup> stores to the store-operated channels. STIM1 has been found to activate two types of store-operated channels, Orai1, which has been reported to mediate the Ca<sup>2+</sup> release-activated Ca<sup>2+</sup>-selective current, ICRAC, and TRPC channels, which conduct the non-voltage activated, non Ca<sup>2+</sup>-selective ISOC current. Despite both Orai and TRPC channels have been found to be activated by STIM1 upon depletion of the intracellular Ca<sup>2+</sup> stores and contribute to conduct SOCE in different cell types, current evidence support that both types of channels have specific and non-overlapping physiological functions.

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## Correlating genomics, proteomics and function through 3D cryo-TEM of intact environmental microbial cells

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Although cryogenic transmission electron microscopy (cryo-TEM) has been available for many years, it has rarely been applied to environmentally-relevant organisms. This in part due to the difficulty in preparing cryogenic TEM samples from microorganisms that cannot be cultured. Cryo-TEM has already changed our view of microbial cell architecture and cryogenic electron tomography (cryo-ET) is becoming a more widely used technique. Consequently, there is a potential interest in using this technology as an approach to study environmental microbial systems. These systems are challenging because they are often remote not possible to culture, difficult to transport artifact-free and intact and "dirty" minerals and nanoparticles although such particles contribute to their interest. We demonstrate that these obstacles can be overcome. Our results include unprecedented cryo-TEM and cryo-ET image data on intact cells and microbial communities from environmental sites for which genomics and proteomics data are available. Correlative high resolution imaging of intact microbial communities integrated with metagenomics and proteomics data can help us understand metabolic states, inter-species relationships, the role of bacteriophage infections and the adaptive responses to external stress. We have established unprecedented interactions and cytoplasmic connections across species in the well characterized AMD community. These first successful applications of cryo-TEM to microorganisms within the in situ context of their mutual interactions and extracellular minerals open the way to similar studies in many other relevant model and environmental systems in microbial ecology, geomicrobiology and plant or biomedical microbial communities.

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