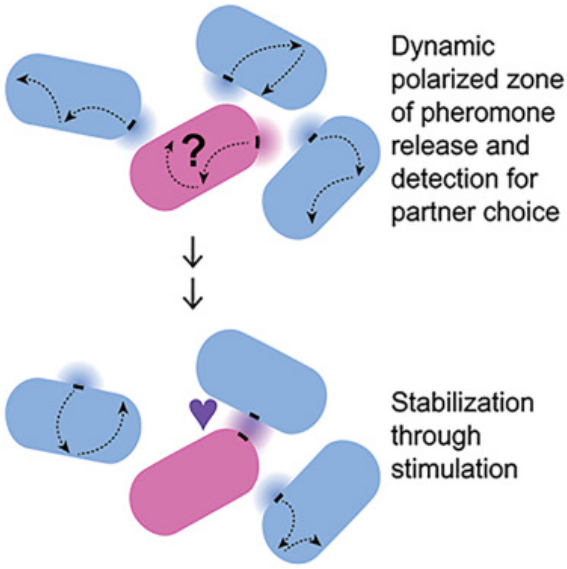
PhD project – Sophie Martin's lab – University of Lausanne, Switzerland

The PhD project will aim to dissect the molecular mechanisms by which eukaryotic cells detect an external gradient of a chemo-attractant and orient their polarity up-gradient. In many situations, cells obtain information about their surrounding by interpreting chemical gradients. These allow them to navigate through directional growth (chemotropism) or directional migration (chemotaxis). For instance, immune cells migrate towards signal released by bacteria or attacked host cells to eliminate pathogens, axons growth towards the source of attractive gradients to form new synaptic connections, sperm cells use chemo-attractants to find the oocyte and amoebae use gradients of cAMP to aggregate into fruiting bodies. In each case, perception of the chemo-attractive signal through G-protein coupled receptors (GPCR) leads to cytoskeletal rearrangement, which produces a directional response.



The project will make use of the fission yeast eukaryotic model, one of simplest, well-characterized eukaryotic cell, which offers excellent genetic and cell biological tools. In this organism, cells exhibit chemotropism during sexual reproduction, when gametes of opposite mating types secrete pheromones. These pheromones are detected by GPCR at the cell surface, which leads to directional growth towards the partner cell. Polarized growth relies on the local activation at the plasma membrane of the small GTPase Cdc42, which locally activates effectors to polarize the cytoskeleton and secretion machinery. Interestingly, upon pheromone detection, Cdc42 first exhibits a period of exploratory dynamics, where zones of activity assemble and disassemble at the cell periphery, exploring the cell's environment (Bendezu and Martin, Current Biology, 2013). These zones are fully-developed sites of polarity, where the pheromones are released and detected. As zones are stabilized by high-level pheromone perception, this has led to a 'speed-dating' model where facing zones in compatible partners are stabilized through stimulation (Merlini et al, Current Biology 2016; see figure). The molecular mechanisms linking pheromone perception to Cdc42 zone dynamics are however unknown. This will be the subject of the PhD research.