Live imaging of collective behavior in cell populations

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Emergent behaviors in cell populations are observed in several cases, i.e. collective migration, patterning in embryos, or the order/disorder transition in epithelial cells. Among these cases, In vitro, under the proper growth conditions, human induced Pluripotent Stem Cells (hiPSCs) form highly symmetric circular structures of polarized cells, dubbed neural rosettes. Neural rosettes mimic the spatial organization found in the early stages of the embryonic neural tube. To study this emergent behavior, we have designed a setup, composed of an epifluorescent microscope and a stage-top CO2 incubator, capable of acquiring 1-2 weeks time-lapse sequences. This setup has a 2 mm field width which allows us to capture the emergence of neural rosettes from the very beginning of hiPSC differentiation. We have generated modified hiPSCs in which the nuclear protein FUS/TLS is expressed in fusion with a red fluorescent protein, tagRFP, resulting in permanent labeling of cell nuclei. In the image analysis, first the fluorescent cell nuclei are detected from each image; then we compute the structure factor and define an order parameter that quantifies the degree of organization and symmetry of the emerging rosettes and characterizes the phase transition of the cell population. Preliminary results indicate that rosettes are emergent cells structures. We also show how live fluorescent markers can be used in flow cytometry analysis to extrapolate information on the growth and the partitioning error of cells.