

## Shape Manifolds for Modelling Cells Undergoing Migration

Nasir Rajpoot (Computer Science) & Anne Straube (CMCB, WMS)

Directional cell migration is of crucial importance during embryonic development and wound healing, while deregulation of cell migration during metastasis is one of the most deadly features of cancer cells. Cell migration involves front protrusion powered by actin polymerisation, retraction of the cell rear by acto-myosin contraction, and traction mediated by integrin-containing adhesion sites that link the cytoskeleton to the extracellular matrix. In addition, it is thought that microtubules play an important role in maintaining cell polarity and steering migration direction.

For cells to reach their destination and desired distribution in the body, they need to communicate with each other and integrate signals from the extracellular space. In this project, we will use human pigment epithelial cells that form a single cell layer in the retina. In culture, these cells distribute evenly on 2D substrates while at the same time maintaining a minimal density. Thus at very low density these cells form colonies, this means that cells with a common ancestor stay together. At higher densities, cells freely explore the 2D space, but their behaviour appears to be guided by several principles rather than randomness. This is based on observations that cells can migrate in a straight line for several hours, thus internal feedback loops can robustly support cell polarity even in the absence of external gradients. However, we do observe that repolarisation and turns are almost always induced upon cell-cell contact or apparently spontaneously.

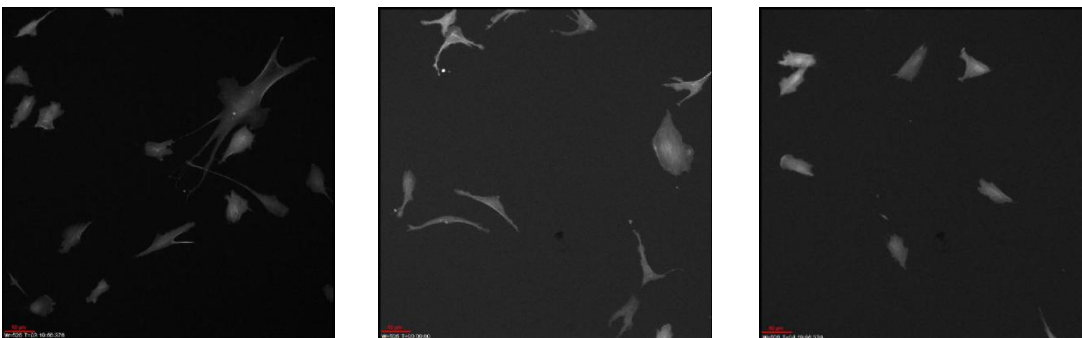


Figure: Snapshots of *in vitro* migrating cells depicting their deformable shape.

As shown in the above Figure, the cells have a dynamic deformable boundary which has been modelled (though at a smaller scale) in the literature using level sets [1] or active contour models, also known as *snakes* [2]. However, a major limitation of these commonplace approaches is that they cannot efficiently handle multiple, possibly overlapping cells. Besides, these models do not directly take into account shape characteristics, rather only boundary and regional constraints are applied.

In this miniproject, you will develop a model-based cell tracking algorithm which will allow tracking cells and detecting contact events in the experimental data already acquired by Anne Straube's lab in CMCB. As a first step, you will study shape manifolds [3] as a suitable model for representing cells. This will involve problem formulation casting it as a shape representation problem, coding the representation using manifold embedding method presented in [3], and conducting experiments on several image sequences acquired by the Straube lab. The second and final step of this miniproject will involve tracking cells using a signature-based matching algorithm [4] where the signatures will be derived from the representation of cell shape manifolds developed in the first step.

A long-term aim of this work is to understand which guidance principles underlie the aforementioned directional decisions in cell migration, taking into account internal structures (e.g. centrosomal position) in addition to tracking cells and contacts. In a possible **PhD project** derived from this miniproject, detection and tracking of intracellular structures and biomarkers relative to the cell boundary could be implemented in order to time cytoskeletal events occurring during spontaneous and contact-induced directional changes. In another related miniproject, we will simulate cell behaviour following certain assumed principles to allow a later comparison of behaviours with experimental data from cells.

### Bibliography:

- [1] Degerman *et al.* (2009) *J. Microscopy*, 233:178–191.
- [2] Zimmer *et al.* (2002) *IEEE Trans. Med. Imaging*, 21(10):1212–1221.
- [3] N. Rajpoot and M. Arif (2009), *Ann. BMVA*, 2008(5):1-15.
- [4] P.C.S. Bangalore-Nagaraj *et al.* (2010), Abstract presented at Bioimaging Informatics, Carnegie Mellon University, Pittsburgh (USA).