Developing new tools for 3D analyses of cell migration

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Actin based cell migration underlies many fundamental biological processes such as development, the immune response, and metastasis. For a number of years we have been developing tools for the 2D analysis of cell motility, and we and others have used these tools to investigate how extracellular stimuli control the coordinated assembly of the actin-myosin cytoskeleton resulting in cell shape changes and forward motion¹. Advances in microscopy techniques now make it possible to study cell migration in 3D, which promises to reveal important details about pattern formation of signaling molecules (phospholipids) in the membrane and how they control actin assembly. In the long run these techniques will allow to study cells in their natural 3D environment which is physiologically more relevant than studying cell migration on a 2D surface

In a collaboration with the Stephens lab (Babraham Institue), which will be funded by the BBSRC from April 2011, we have recently obtained high quality experimental data of neutrophil motility in 3D (still on a 2D surface) and were able to do 3D volume reconstructions. In the current miniproject we now want to develop new tools for tracking cell boundary movements in 3D, and find appropriate ways for creating parameterized maps thus enabling statistical analysis of spatio temporal patterns obtained from many cells.

In a recent Systems Biology miniproject we developed a new 2D method for mapping regions of the cell boundary between one frame of an image time-series and the next². This method is computationally much faster and results in a more homogeneous mapping when compared with previously used level set and active contour methods for tracking cell boundaries. In the current miniproject this method will be extended to 3D.

Different techniques for surface parameterization will be explored as to how they can be used to create meaningful maps of the spatio-temporal dynamics.

Both parts require programming skills in either Matlab, C++, or Java, and basic knowledge of numerical methods as well as an interest in visualization techniques. There are a number of options for a subsequent PhD project and we are currently discussing possible joint projects with Charlie Elliott (Mathematics) who also has a strong interest in boundary tracking and membrane dynamics.

¹ L. Bosgraaf, P.J.M. van Haastert, T. Bretschneider. <u>Analysis of cell movement by simultaneous quantification of</u> local membrane displacement and fluorescent intensities using Quimp2. Cell Motility and the Cytoskeleton, 66(3):156-165, 2009. ² R.A. Tyson, D.B.A. Epstein, K.I. Anderson, T. Bretschneider. <u>High resolution tracking of cell membrane dynamics in</u>

moving cells: An electrifying approach. Math. Model. Nat. Phenom., 5(1):34-55, 2010.