Erik Sahai – Modelling cancer cell invasion in complex environments

The acquisition of invasive behaviour enables the tumour cells to move into either the surrounding tissue or the vasculature and thereby spread to other parts of the body. Cell migration depends on the complex interplay of actin polymerisation, deformation of the plasma membrane, actomyosin contractility, and cell-matrix adhesion. Recent work has revealed that cancer cells can use different migratory strategies, particularly when challenged with complex three-dimensional matrices in vivo. Further the mode of cell migration determines the sensitivity of invading cancer cells to interventions that target either regulators of actin polymerisation or actomyosin contractility. This presents a particular problem when attempting to extrapolate findings from simple *in vitro* experiments to the complex matrix environments that surround tumours. To address this we have developed an agent based-finite element model of cell motility within different ECM topologies. This enables the optimal migration strategy and response to anti-invasive agents in different matrix geometries to be predicted. Different migratory strategies are predicted to be most effective depending on the matrix geometry. Further, plasticity (that is switching between migratory strategies when the environment changes) is an emergent property of the model. We will present analysis of the underlying causes of this behavior together with testing of model predictions by intravital imaging of melanoma.