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From Crawlers to Swimmers — Mathematical and Computational Problems in Cell Motility

Cell locomotion is essential for early development, angiogenesis, tissue regeneration, the immune response, and wound healing in multicellular organisms, and plays a very deleterious role in cancer metastasis in humans. Locomotion involves the detection and transduction of extracellular chemical and mechanical signals, integration of the signals into an intracellular signal, and the spatio-temporal control of the intracellular biochemical and mechanical responses that lead to force generation, morphological changes and directed movement. While many single-celled organisms use flagella or cilia to swim, there are two basic modes of movement used by eukaryotic cells that lack such structures – mesenchymal and amoeboid. The former, which can be characterized as 'crawling' in fibroblasts or 'gliding' in keratocytes, involves the extension of finger-like filopodia or pseudopodia and/or broad flat lamellipodia, whose protrusion is driven by actin polymerization at the leading edge. This mode dominates in cells such as fibroblasts when moving on a 2D substrate. In the amoeboid mode, which does not rely on strong adhesion, cells are more rounded and employ shape changes to move – in effect 'jostling through the crowd' or 'swimming'. Here force generation relies more heavily on actin bundles and on the control of myosin contractility. Leukocytes use this mode for movement through the extracellular matrix in the absence of adhesion sites, as does Dictyostelium discoideum when cells sort in the slug. However, recent experiments have shown that numerous cell types display enormous plasticity in locomotion in that they sense the mechanical properties of their environment and adjust the balance between the modes accordingly by altering the balance between parallel signal transduction pathways. Thus pure crawling and pure swimming are the extremes on a continuum of locomotion strategies, but many cells can sense their environment and use the most efficient strategy in a given context. We will discuss some of the mathematical and computational challenges that this diversity poses.