A theoretical model for focal adhesion and cytoskeleton formation in non-motile cells

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Abstract:
To function and survive cells need to be able to sense and respond to their local environment through mechanotransduction. Crucially, mechanical and biochemical perturbations initiate cell signalling cascades, which can induce responses such as growth, apoptosis, proliferation and differentiation. At the heart of this process are actomyosin stress fibres (SFs), which form part of the cell cytoskeleton, and focal adhesions (FAs), which bind this cytoskeleton to the extra-cellular matrix (ECM). The formation and maturation of these structures (connected by a positive feedback loop) is pivotal in non-motile cells, where SFs are generally of ventral type, interconnecting FAs and producing isometric tension. In this study we formulate bio-chemo-mechanical continuum models (in both one and two spatial dimensions) to describe the coupled formation and maturation of ventral SFs and FAs. We use a set of reaction–diffusion–advection equations to describe three sets of biochemical events: t he polymerisation of actin and subsequent bundling into activated SFs; the formation and maturation of cell–substrate adhesions; and the activation of signalling proteins in response to FA and SF formation. The evolution of these key proteins is coupled to a viscoelastic description of the cell cytoplasm and the ECM. We employ this model to understand how cells respond to external and intracellular cues in vitro and are able to reproduce experimentally observed phenomena including non-uniform cell striation and cells forming weaker SFs and FAs on softer substrates.