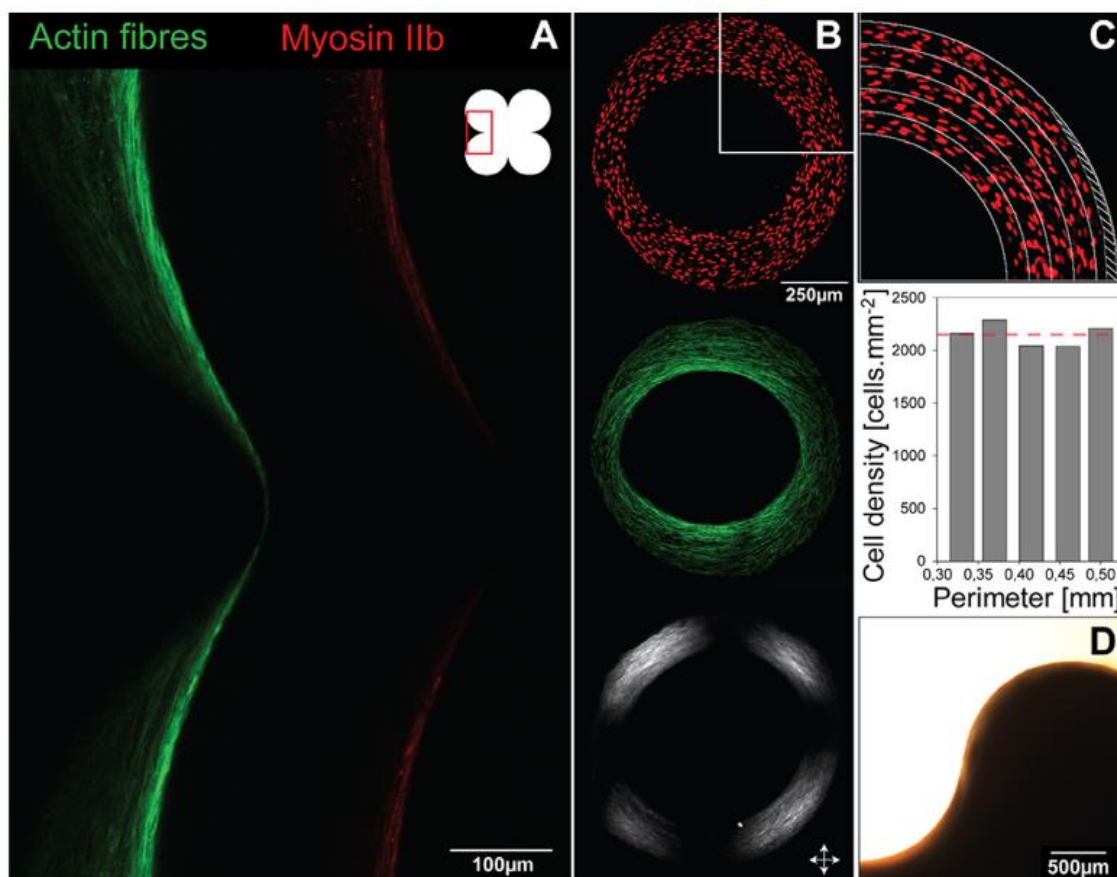


# How Linear Tension Converts to Curvature: Geometric Control of Bone Tissue Growth

## Abstract

This study investigated how substrate geometry influences in-vitro tissue formation at length scales much larger than a single cell. Two-millimetre thick hydroxyapatite plates containing circular pores and semi-circular channels of 0.5 mm radius, mimicking osteons and hemi-osteons respectively, were incubated with MC3T3-E1 cells for 4 weeks. The amount and shape of the tissue formed in the pores, as measured using phase contrast microscopy, depended on the substrate geometry. It was further demonstrated, using a simple geometric model, that the observed curvature-controlled growth can be derived from the assembly of tensile elements on a curved substrate. These tensile elements are cells anchored on distant points of the curved surface, thus creating an actin “chord” by generating tension between the adhesion sites. Such a chord model was used to link the shape of the substrate to cell organisation and tissue patterning. In a pore with a circular cross-section, tissue growth increases the average curvature of the surface, whereas a semi-circular channel tends to be flattened out. Thereby, a single mechanism could describe new tissue growth in both cortical and trabecular bone after resorption due to remodelling. These similarities between in-vitro and in-vivo patterns suggest geometry as an important signal for bone remodelling.



**Figure 6. Tissue organisation.** A - Tissue produced in a pore made of 4 adjacent circles and stained for actin stress fibres and myosin IIb. Actin fibres colocalised with myosin IIb are present on the whole surface but their higher density on concave interfaces suggests a local higher stress state of the cells. B - Tissue is made of cells and collagen. Nuclei (red), actin stress fibres (green) and collagen fibres (visualized by polarized microscopy) are oriented parallel to the interface. The white arrows show polarisation direction. C - The homogeneous distribution of nuclei shows that cell density is independent of geometry and suggests a local dependence of cell proliferation on the local curvature. D - An example of a convex HA surface (D35) on which only a mono-layer of tissue was formed.  
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