Multiscale modelling of the mechanics of solid tumours and interactions with the host tissue

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The tumour microenvironment is now widely accepted as being an important factor in the proliferation, invasion and metastasis of cancerous cells [1]. In particular, it has been shown that the mechanical interaction between cells and the extracellular matrix (ECM) plays an important role in regulating cell proliferation. The exact physical mechanisms producing this effect are currently unknown, thus motivating the development of physiologically accurate biomechanical models to compare with experimental data. To our knowledge, there are no models accounting explicitly for components of the tumour microenvironment. This work focuses on developing a novel numerical methodology to simulate a spherical tumour expanding into a collagen fibre network and thus explicitly model tumour-ECM interactions.

The tumour is represented as a nonlinear solid at the macroscopic (tissue) scale, while the fibre network, embedded in an elastin matrix, is discretised at the microscopic (fibre) scale. A 3D finite element method was utilised for the macroscopic scale, with the microstructure represented by a 3D fibrillar network at each integration point. An explicit Total Lagrangian solver was employed at both scales. Volume-averaging theory [2] was used to couple the fibre network properties --- such as collagen fibre density and architecture --- to the tissue scale. This enabled the macroscopic boundary conditions due to tumour growth to be translated to the microstructure. The growth itself was driven by a single chemical factor that was considered to have constant concentration with respect to the growth time scale. To include the effect of compressive stress on tumour growth, a simple expression relating the pressure at the tumour-ECM boundary to the rate of growth was implemented.

The proposed numerical model was informed by and compared to *in vitro* tumour spheroid data obtained by the authors. The efficiency, robustness and scalability of the multiscale algorithm was assessed through tumour growth numerical simulations of spheroidal geometries.

[1] The microenvironment of the tumour-host interface, Liotta, LA and Kohn, EC, Nature (2001) Vol 411, Issue 6835, 375-379
[2] Volume-averaging theory for the study of the mechanics of collagen networks, Stylianopoulos, T and Barocas, VH, Comput. Methods Appl. Mech. Engrg (2007) 196:2981-2990