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Evolution of tumor spheroids: adopting a Bingham scheme for the cell component

Avascular multicellular spheroids are the simplest form of tumours that can be studied experimentally under controlled conditions. They can be grown in suspensions (thus being subject to atmospheric pressure) or in a gel which offers some mechanical resistance to their expansion. They are made of proliferating cells, quiescent cell and of dead cells progressively degrading to liquid. The whole cell population is embedded in an extracellular fluid, which provides the mass required for cell replication.

During the last years it has become evident that, despite the advantage offered by the simple geometry, the problem of describing the growth (or even the steady state) of a multicellular spheroid is generally very complicated and requires the choice of constitutive equations for the mechanical behaviour of the system. A peculiar difficulty is originated by its composite nature. Various papers have been devoted to the problem of spheroids evolution, assigning an important role to the deformability of the system of mutually interacting cells by introducing interaction potentials (depending on the cell volume fraction) and constitutive laws that may include yield stress and elasticity (see [1]).

Here we want to present an evolution model in which the main assumptions are:

(i)the cell volume fraction in the viable region is constant,

(ii)the rheological properties of the set of cells in the viable zone are the ones of a Bingham fluid,

(iii)the only species considered in the cells metabolism is oxygen and the influence of metabolites is neglected.

Thus our model is in the context of the two-fluid approach. The inspiring criterion was to incorporate some physically relevant feature (as it can be the presence of intercellular links providing a stress threshold for flow), but introducing the minimum possible number of constitutive quantities. Formulating a Bingham-like scheme proved to be not so simple, since some classical models are not compatible with velocity fields that have necessarily to occur in the case of a growing spheroid. Thus this aspect of the analysis is particularly delicate. The spheroid evolution is followed from the initial fully proliferating phase, to the stage which includes a necrotic liquid core, possibly reaching an asymptotic equilibrium (the existence of steady states has been studied in the same framework in the paper [2]). Despite the many simplifications (to which we add some less important assumptions, like the existence of interfaces separating the various classes of cells), the problem turns out to be considerably complicated. An existence theorem and numerical simulations will be presented.

References

[1] D. Ambrosi, L. Preziosi. Cell adhesion mechanisms and stress relaxation in the mechanics of tumours. Biomech. Model. MechanoBiol. 8 (2009) 397-413.
[2] A. FASANO, M. GABRIELLI, A. GANDOLFI. Investigating the steady state of multicellular spheroids by revisiting the two-fluid model. To appear on Math. Biosci. Eng.