Exploration of Cell Assisted Cell Growth

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An elegant example of a transition between different forms of collective behavior in living matter is investigated under non-starvation conditions in the model eukaryote, *Dictyostelium discoideum*. Specially, we explore the change between lag and log growth well known in practical cell culture. We will discuss models for such a transition that describe it as much more than a delayed recovery from a change in environment, as it is sometimes regarded, but rather as an effect simply dependent on cell density. A critical issue we confront is the means by which cells communicate their presence to other cells in order to stimulate growth.

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Aside from the challenges of massively parallel cell culture encountered in contemporary drug or toxicity screening, the question of the extent to which cells promote cell growth in colonies is a basic problem of multicellularity in biology. In this experimental program we have confronted the problem in different environments: the traditional vessels for cell-culture: tens of ml volume cultures in well shaken flasks as well as highly confined microfluidic chambers with volumes four orders of magnitude smaller. The later system affords the possibility of highly controlled fluid motion. We have been using these systems to explore the familiar transition from slow (lag phase) to fast (log phase) growth in a familiar eukaryote, *Dictyostelium discoideum.* We find that the transition can be simply regarded as a density effect with quantitatively similar behavior although the hydrodynamic environments can be dramatically different: our shaker cultures are well mixed and the microchamber systems are used in both advection and diffusion dominated regimes. Such variations are critical as we explore collective growth models quantitatively that treat intercellular interaction as being due to cell contact or via small molecule intermediaries. Our measurements appear to rule out the later possibility. We have discovered that the presence of a substrate can have a dramatic effect on the structure of colonies at high densities. Finally, we find that while a straightforward Landau expansion in density fails to describe the transition, fluctuation assisted growth can be readily discussed in mean field theory in order to confront the transition. Within the long-range signaling theory, the fluctuations arise from the chemical equilibrium of binding to cell surface receptors and the vital fluctuations in the contact model can be readily discussed for well mixed cultures via simple colloidal hydrodynamics.

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