Description for a problem studied at the Virtual Physiological Human Network of Excellence Study Group
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< http://www.maths-in-medicine.org/vph-noe/2009/doming-epithelial-cells/ >

Modelling doming in epithelial cells: physical properties of epithelial cells that permit doming and differences in cells in domes compared to non-doming neighbours?

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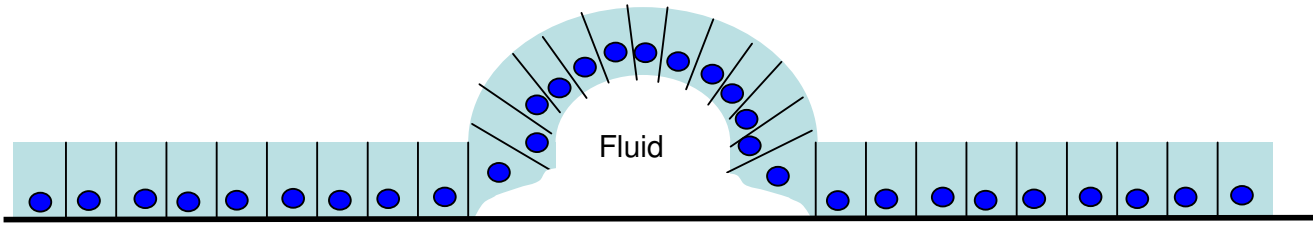
When grown on rigid substrates in confluent monolayers, MDCK and other epithelial cell lines form “dome” structures. These domes are formed by cells that lifte up from the solid support but are continuous with the monolayer (as represented in the schematic below). There is sporadic data in the literature about signalling pathways that control this behaviour and I list a few of the more recent data at the end, but very little is known about this process. When grown on flexible, semi-permeable filters, domes are not formed. What seems well established is that Na^+/K^+-ATPase activity is crucial for dome formation suggesting that ion transport and associated water flow are important.



Solid substrate

We have monitored domes over many hours in MDCK cells and found specific mutants that alter the size and dynamics of the domes. Two movies for two different mutant cells are included on the CD. These are the same cell type but they differ in the expression of a fluorescent protein we introduced stably. We found that domes grow, then collapse, and usually re-form in the same place. The challenge I would like to pose to the group is to develop a model that describes doming behaviour using the provided movies as source for data about the physical dimensions of domes relative to cells, the speed and patterns of re-arrangements that accompany dome formation.

The model should take into account the cellular parameters that have to be altered to generate the different domes in the two mutants. The kinds of parameters that should be included in the model are adhesion between cells, adhesion between cells and the substrate, the permeability of the cellular junctions, cellular stretchiness (for lack of a better term). (We plan to measure rigidity using Atomic Force microscopy, and possibly cell adhesion in the future, but will not have this data available until late in the year). Another question that is relevant in this context is whether or in what way cells surrounding a dome are different from those further away from it.

The physiological relevance relates to the fact that many steps in development and tissue rearrangement in disease may be initiated by such shape changes in tissue and we understand very little about the kinds of "mechanical" parameters that have to change to allow this behaviour. Now that we have means to measuring these parameters directly, a model that points to the kinds of cellular properties we should be measuring would be immensely useful.

We supplied two movies that show the dyamic behaviour of two difference clones of MDCK cells. The width of the image in each movie is 675µm. so that should allow you to use the actual dimensions of cells etc. in the model.

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