Living liquid crystals

The paper in brief

- Epithelial tissues line the cavities and surfaces of organs throughout the body.
- Such tissues remove unnecessary or disease-causing cells through an extrusion process.
- Saw *et al*.[1] (page XXX) have modelled the epithelium as a type of liquid crystal.
- They report a universal correlation between extrusion sites and positions of topological defects in the liquid crystal.
- The work opens up opportunities for further studies into the feedback between the cellular arrangement within tissues and key biological processes.

Biological matters arising

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Epithelia must continuously renew to carry out their barrier function. Previous work[7,8] established that epithelia have a preferred cell density that is maintained through a balance between cell division and removal (which occurs through extrusion). But why some cells are targeted for removal rather than others was mysterious. Saw and colleagues' explanation adds to a growing body of evidence showing the feedback between physical effects, mechanical forces, and biological behaviour.

The constituent units of nematic liquid crystals are elongated and show orientational order. Similarly, migrating cells generally possess a long axis, and the direction of movement of adjacent cells is closely correlated. Saw *et al*. show that defects similar to those of nematic liquid crystals occur in epithelia, that the stress distributions around the defects are similar to those in nematics, and that the location of extrusions correlates closely with one category of defect (known as +1/2 defects). Epithelia thus seem to behave much like liquid crystals.

What molecular mechanisms underlie the nematic-like behaviours of cells? Intercellular adhesion has a crucial role in coordinating the collective migration of cells, thus ensuring high orientational order — a fundamental property of nematics. Consistent with this, Saw and co-workers observed that reducing intercellular adhesion between epithelial cells reduces orientational order and leads to an increase in defects and extrusions.

Cell extrusions have previously been shown to often be the result of signalling events that take place over several hours[9]. An open question therefore arising from the current work is how long cells must reside close to a defect to trigger extrusion. Furthermore, the authors' observation that extrusions occur in the vicinity of one type of nematic topological defect but not near other types of defects is puzzling and comparison of the different types of defects will likely be very informative for understanding the link between tissue topology, mechanical stimuli and cell fate.

More generally, this discovery reflects a continuing trend for transposing theories developed for non-living systems to biological materials. Presently, it is unclear whether liquid crystals and epithelia are truly close analogues, or whether cell-specific adjustments to the theory of nematics will be necessary to fully explain cell dynamics within tissues in this framework. Nevertheless, the concept of cellular nematics offers an exciting theoretical framework that provides a link between organization at the tissue-scale and the behaviour of single cells. As such, it might be useful in many areas of biology.

For example, extrusions are commonplace during embryonic development. Is the spatial location of these extrusions solely controlled by genetics, or does local tissue organization also participate? The new findings are also potentially relevant to other developmental processes and to cancer, which involve a phenomenon called cell competition. This occurs when two cell populations vie for domination and the losing cells are extruded from the epithelium. Can cell competition be understood as a mixing event between two different nematic liquid crystals? And could the winning population be predicted purely on the basis of differences in the nematic properties of the two populations?

Finally, Saw and colleagues' discovery might help us understand the epithelial-to-mesenchymal transition (EMT), an early event in cancer progression that is linked to a

reduction in intercellular adhesion and an increase in cell motility. Given that both intercellular adhesion and cell motility probably influence the properties of epithelial-cell nematics, it would be intriguing to know how the molecular steps leading to EMT affect such liquid crystals.

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Figure 1 | Defects in nematic systems of epithelial cells. Saw *et al*.[1] report that epithelial cells align in a manner similar to the molecules in nematic liquid crystals, and that defects in the liquid-crystal structure correlate with locations at which cells are extruded from the cell system. **a**, This micrograph shows a defect in a layer of epithelial cells. The orientation of the cells is indicated with red lines. **b**, The orientations of the cells correspond to a comet-shaped defect known to occur in nematic liquid crystals, called a +1/2 defect.