

2531cs1102

Understanding the physical forces shaping early embryos

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ProjectID	2531cs1102
Project title	Understanding the physical forces shaping early embryos
EPSRC theme	Physical Sciences
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Standard or collaborative project	Standard project
Restrictions for candidates applying	Only Home fees candidates can apply

Project summary

One of the most striking properties of embryos is the complex shape changes that they undergo during morphogenesis. The physics of foams has been remarkably successful at predicting the shape of small cell aggregates, such as early embryos, from the distribution of tension at cellular interfaces.

Shaping a developing embryo requires spatiotemporal changes in surface tension distributions. One fundamental property of living cells is their ability to actively modulate the tension at their surface in seconds through controlled biochemical reactions. Despite the importance of surface tensions for embryonic development, our understanding of the molecular basis of surface tension control in cells remains incomplete, partly because of challenges in characterizing them experimentally.

This project will address this knowledge gap thanks to new biophysical approaches. We will use Atomic Force Microscopy to measure tension at free surfaces, newly-developed DNA nanotechnology to directly quantify tension at cell-cell contacts, and confocal microscopy to image aggregate shape.

Aim 1 will validate the application of foam theory by directly measuring tension at free surfaces, tension at cell-cell contacts, and shape.

Aim 2 will determine how tension at cell-cell contacts evolves in response to a change in tension at free surfaces. For this, we will modulate free surface tension with optogenetics and image the resulting change in aggregate shape. We will characterize change in free surface tension by AFM and measure cell-cell tension using DNA-based force sensors. After characterizing the normal response, we will deplete proteins involved in force transmission between cells and determine how this affects aggregate shape change.

Aim 3 will search for proteins whose enrichment correlates with tension at the different cellular surfaces. This information will enable semi-quantitative measurement of dynamic tension changes with microscopy.

Overall, this project will allow to decipher the molecular and biophysical mechanisms that control the shape of multicellular aggregates.