Title: Mathematical modelling of cytoneme-based biochemical signalling

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Project:

Cytonemes are cellular protrusions that enable long distance communication between cells. They are implicated in establishing the morphogenetic gradients associated with pattern formation during development [Brunt et al., 2021], in the growth of gastric tumours [Routledge et al., 2022], and have recently been suggested to promote synapse formation in neurons. Despite their pivotal role in such important physiological processes, cytonemes have received relatively little mathematical treatment. In this project, we will use a combination of mathematical modelling and data analysis techniques to determine the signalling properties of cytonemes that are relevant for tissue patterning and tumour growth.

The mathematical models developed in the project will be based on a PDE-formulation and will build on recent work describing tissue patterning in growing domains [Wedgwood & Ashwin, 2022]. The models will describe the dynamics of two processes. The first will be the growth and retraction of the cytonemes and hence the dynamics of long-range signalling. The second will be the mechanical forces underlying the growth of the biological tissue. These mechanical forces are generated by the movement of cells which, in turn, is dependent on the degree of signalling across the tissue. As such, the tissue growth dynamics are tightly coupled to the cytoneme dynamics. Data to parametrise the models of both processes, some of which are shown in the figure below, will be available through our experimental partner Dr Steffen Scholpp.

Brunt, L., Greicius, G., Rogers, S., Evans, B. D., Virshup, D. M., Wedgwood, K. C. A., & Scholpp, S. (2021). Vangl2 promotes the formation of long cytonemes to enable distant Wnt/β-catenin signaling. Nature Communications, 12(1).

Routledge D., Rogers S., Ono Y., Brunt L., Meniel V., Tornillo G., Ashktorab H., Phesse T. J., & Scholpp, S. (2022). The scaffolding protein flot2 promotes cytoneme-based transport of wnt3 in gastric cancer. eLife, 11:e77376.

Wedgwood K. C. A & Ashwin P. (2022), Morphogen-directed cell fate boundaries: slow passage through bifurcation and the role of folded saddles. Journal of Theoretical Biology, 549:111220.