Morphogenetic biomechanics of mouse hindbrain neuropore closure

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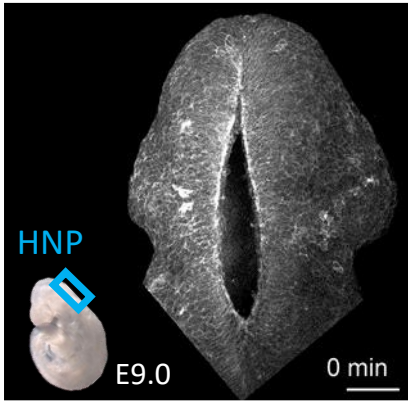


Background

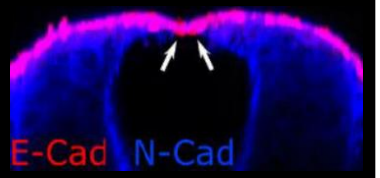
- Neural tube defects affect 1:1000 births worldwide.
- Failed hindbrain neuropore (HNP) closure causes fatal exencephaly.

How are the forces required for HNP closure generated?

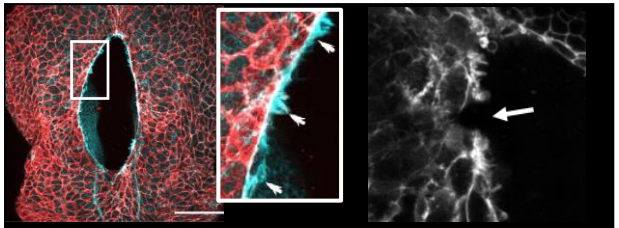
Methods:

Morphometrics, mouse embryo live-imaging, cell-based physical modelling[1]

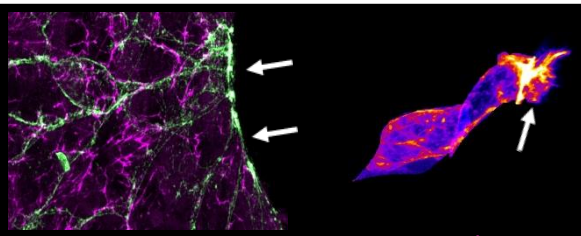
$$E = \frac{1}{2}\sum_{\alpha} K(A_\alpha - A_0)^2 + \frac{1}{2}\sum_{\alpha} \Gamma(P_\alpha - P_0)^2$$



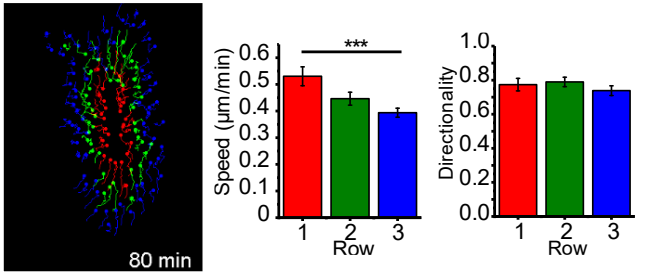
1. Actin cables withstand high tension



2. SE cells attach on ECM at the HNP rim



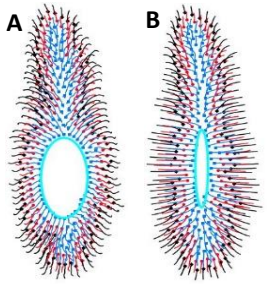
3. SE cells crawl inwards



4. Model iterations based on biology

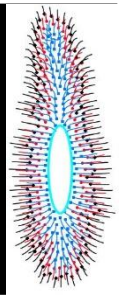
A. Cable constriction alone produces a circular HNP.

B. Cell crawling alone produces a 'slit-like' HNP.



5. Final model

Combining cable constriction and crawling reproduces in *vivo* closure dynamics.



Study significance

- Uncovered cellular mechanisms of mouse HNP closure.
- Biophysical characterisation of a clinically-important developmental process.

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wellcome

[1] E. Maniou, M. F. Staddon, A. Marshall, N. D. E. Greene. A. J. Copp, S. Banerjee, G. L. Galea, Hindbrain tissue geometry determines asymmetric cell-mediated closure dynamics, BioRxiv 2020.