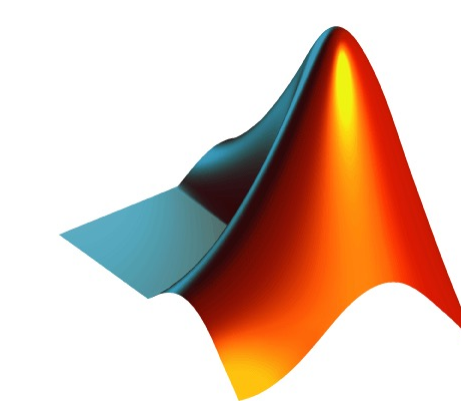


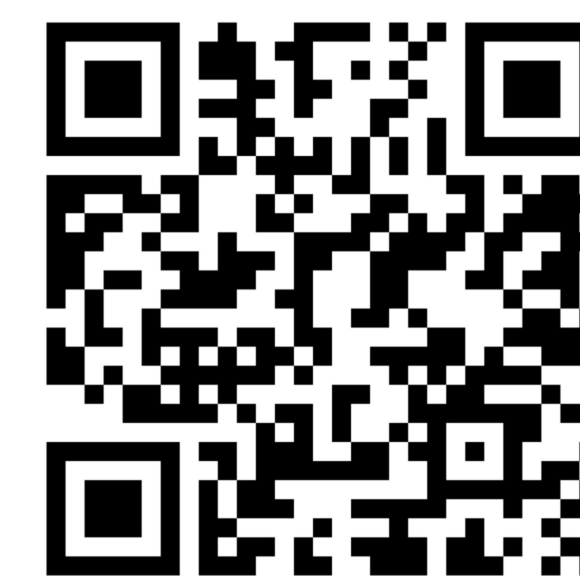


# Learning developmental mode dynamics of single-cell trajectories



Nicolas Romeo<sup>1,2</sup>, Alasdair D. Hastewell<sup>1</sup>, Alexander Mietke<sup>1</sup>, Jörn Dunkel<sup>1</sup>

<sup>1</sup>Department of Mathematics, <sup>2</sup>Department of Physics, Massachusetts Institute of Technology



<https://doi.org/10.7554/eLife.68679>

Embryogenesis is a multiscale process during which developmental symmetry breaking transitions give rise to complex multicellular organisms. Recent advances in high-resolution live-cell microscopy provide unprecedented insights into the collective cell dynamics at various stages of embryonic development. This rapid experimental progress poses the theoretical challenge of translating high-dimensional imaging data into predictive low-dimensional models that capture the essential ordering principles governing developmental cell migration in complex geometries. Here, we combine mode decomposition ideas that have proved successful in condensed matter physics and turbulence theory with recent advances in sparse dynamical systems inference to realize a computational framework for learning quantitative continuum models from single-cell

imaging data. Considering pan-embryo cell migration during early gastrulation in zebrafish as a widely studied example, we show how cell trajectory data on a curved surface can be coarse-grained and compressed with suitable harmonic basis functions. The resulting low-dimensional representation of the collective cell dynamics enables a compact characterization of developmental symmetry breaking and the direct inference of an interpretable hydrodynamic model, which reveals similarities between pan-embryo cell migration and active Brownian particle dynamics on curved surfaces. Due to its generic conceptual foundation, we expect that mode-based model learning can help advance the quantitative biophysical understanding of a wide range of developmental structure formation processes.

## Motivation and Context

Light-sheet microscopy data provides single-cell trajectories across developmental events. However, this is about  $\sim 4 \cdot 10^6$  degrees of freedom.  
→ Necessity to reduce data to a compact representation.  
→ To benefit from physical insight, we use harmonic functions as a representation basis.

We illustrate our approach on zebrafish gastrulation data (Shah et al, *Nat. Comm.* 2019)

## Coarse-graining on curved spaces

We coarse-grain using convolution kernels. The zebrafish embryo has a natural spherical geometry. To satisfy mass conservation, we find families of tensor kernels  $K_0, [K_1]_{j'}^k$  which satisfy

$$\rho(\mathbf{r}, t) = \sum_{\mu} K_0(\mathbf{r}, \mathbf{r}_{\mu}(t))$$

$$J^k(\mathbf{r}, t) = \sum_{\mu} [K_1(r, r_{\mu}(t))]_{j'}^k v_{\mu}^{j'}(t)$$

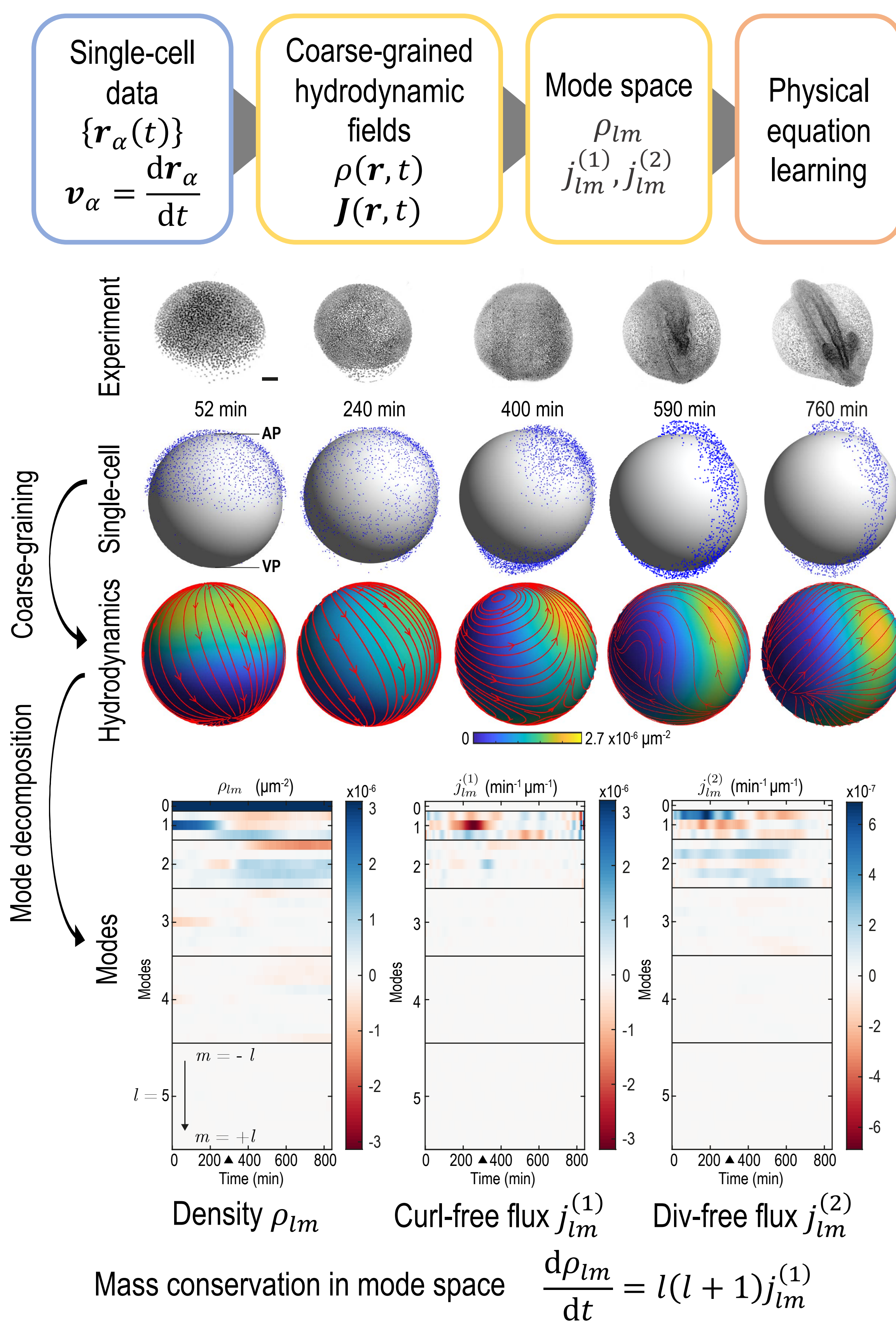
$$\partial_{j'} K_0 = -\nabla_k [K_1]_{j'}^k$$

## Mode decomposition

We use scalar and vector spherical harmonics to reduce fields to a finite number of modes  $\{\rho_{lm}, j_{lm}^{(1)}, j_{lm}^{(2)}\}$ . The resulting spectra are sparse and smooth, with x1800 compression.

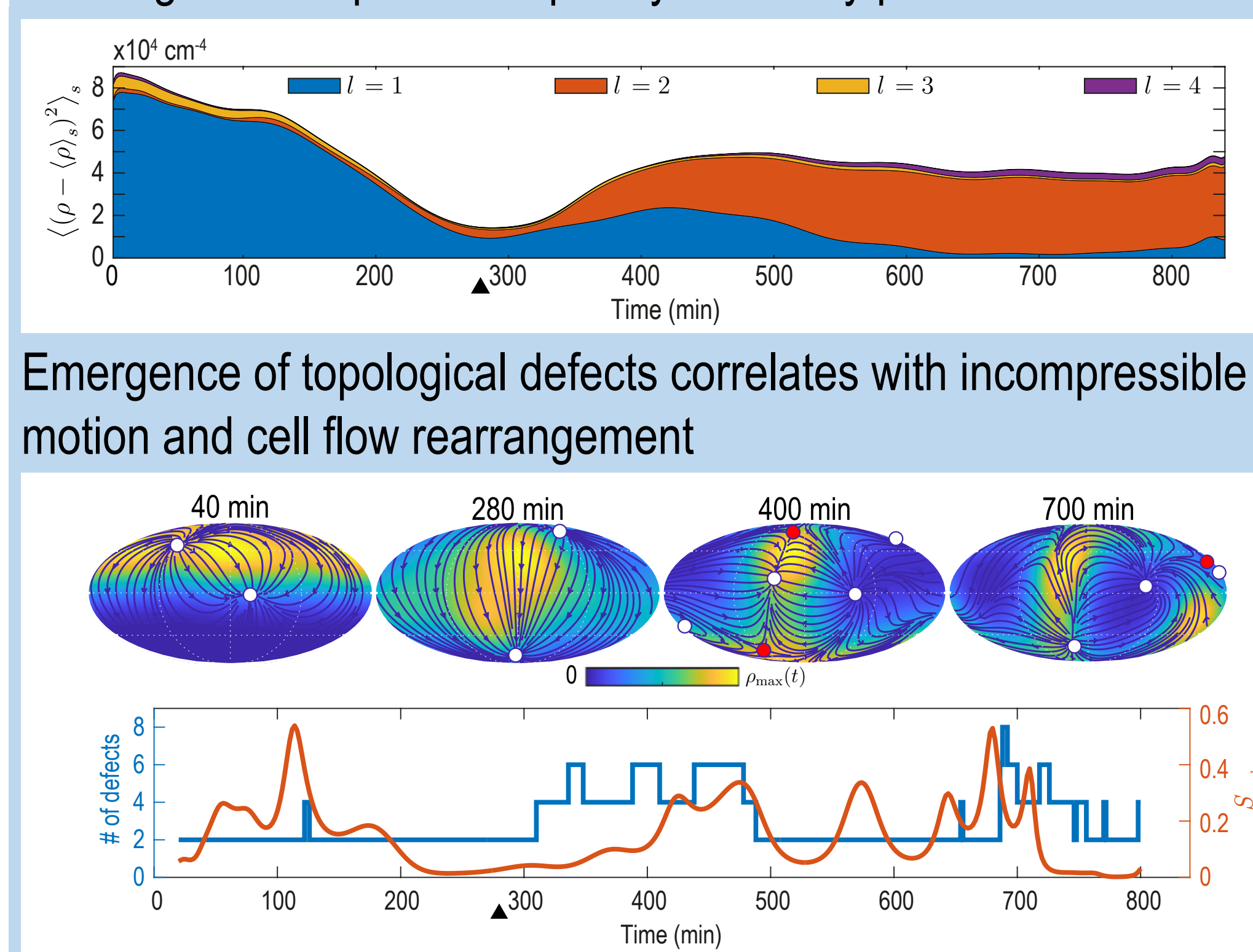
$$\rho(\mathbf{r}, t) = \sum_{l=0}^{l_{\max}} \sum_{m=-l}^l \rho_{lm}(t) Y_{lm}(\mathbf{r})$$

$$\mathbf{J}(\mathbf{r}, t) = \sum_{l=0}^{l_{\max}} \sum_{m=-l}^l j_{lm}^{(1)}(t) \Psi_{lm}(\mathbf{r}) + j_{lm}^{(2)}(t) \Phi_{lm}(\mathbf{r})$$



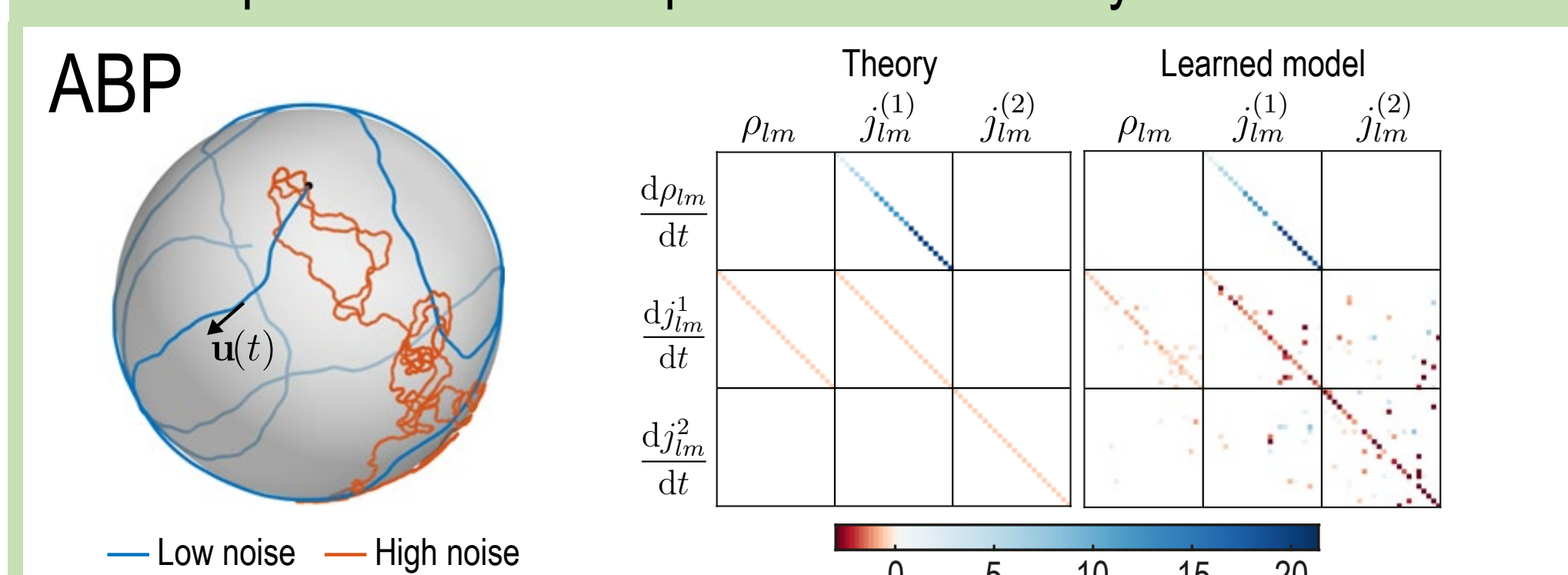
## Insights from mode representation

Average density fluctuations  $\langle(\rho - \langle\rho\rangle)^2\rangle = \sum_{lm} \rho_{lm}^2$   
- Robust identification of developmental phases  
- Emergence of spatial complexity in density patterns



## Validation and comparison: Active Brownian Particles

Active Brownian particles on a sphere have a microscopic dynamic which has an analytic continuum coarse-grained model → Used to test inference code  
→ Example non-trivial coupled linear mode dynamics



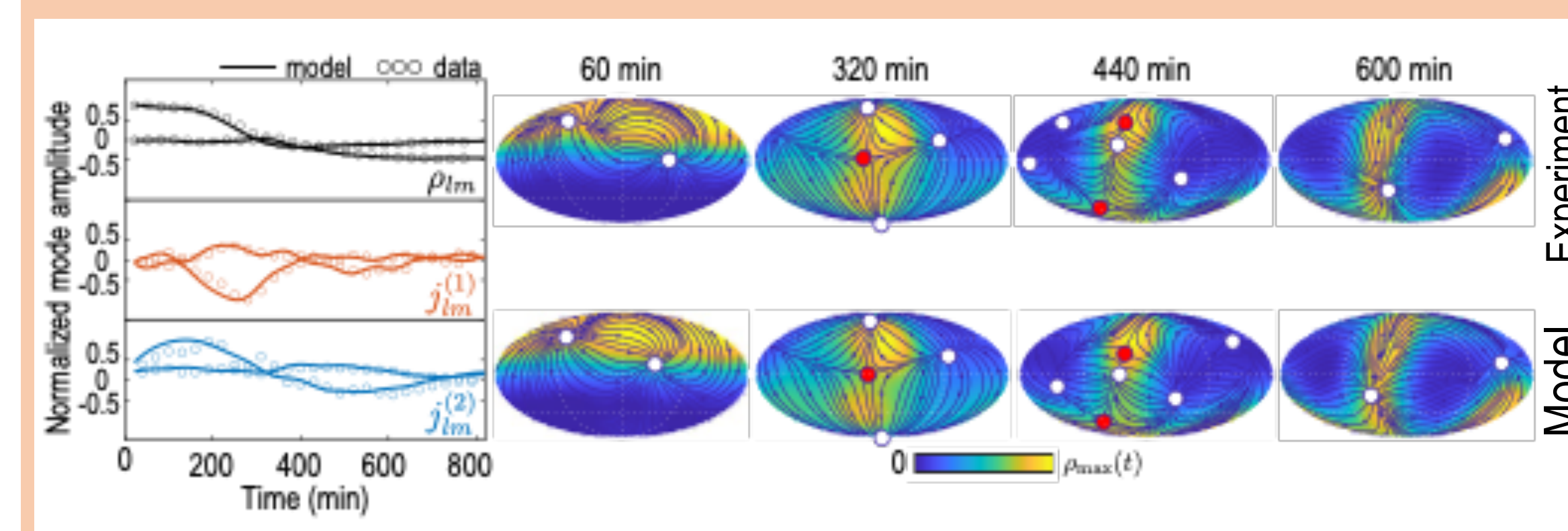
## Mode dynamic inference

No neural networks!

We seek closed dynamics involving the modes  $\{\rho_{lm}, j_{lm}^{(1)}, j_{lm}^{(2)}\}$ .  
As proof of concept, we find a constant-coefficient matrix  $M$  which best fits the observed dynamics:

$$\frac{d}{dt} \begin{pmatrix} \rho_{lm} \\ j_{lm}^{(1)} \\ j_{lm}^{(2)} \end{pmatrix} = M \cdot \begin{pmatrix} \rho_{lm} \\ j_{lm}^{(1)} \\ j_{lm}^{(2)} \end{pmatrix}$$

The models reproduce the data in mode and real space; they are stable and have predictive power for different initial conditions.



$$\begin{cases} \partial_t \rho = -\nabla_k J^k \\ \partial_t J^k = -\frac{\omega_0^2}{2} \nabla^k \rho - D_r J^k \end{cases}$$

$\omega_0$  particle speed  
 $D_r$  noise amplitude

We find that the learned zebrafish model shares some structure with ABPs

## Zebrafish

