TOPOLOGICAL TECHNIQUES TO QUANTIFY BIOLOGICAL PATTERN FORMATION

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{Peter-verreussel, iStock, pbs.org/wgbh/nova/article/zebrafish-sleep/}

Zebrafish (*Danio rerio*)

Wild type: striped pattern

Mutants: variety of patterns

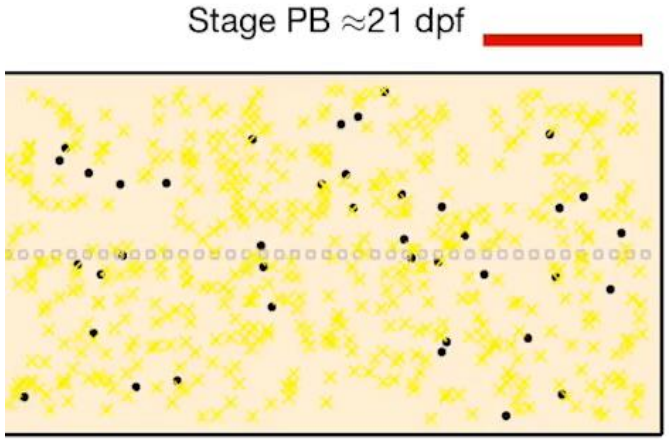
BIOLOGICAL BACKGROUND

{Fish images: https://www.deccanherald.com/spectrum/science/zebrafish-emerging-research-model-671035.html, Frohnhöfer *et al. Biol Open* 2016, Irion *et al. eLife* 2014, Fadeev *et al. eLife* 2015, Singh et al. *Curr Biol* 2015, Courtesy of Uwe Irion & Christiane Nüsslein-Volhard, Video: Yamaguchi et al. *PNAS* 2007}

- Independent cells interacting in the plane
  - Three cell types, two of them with two subtypes, for a total of five types

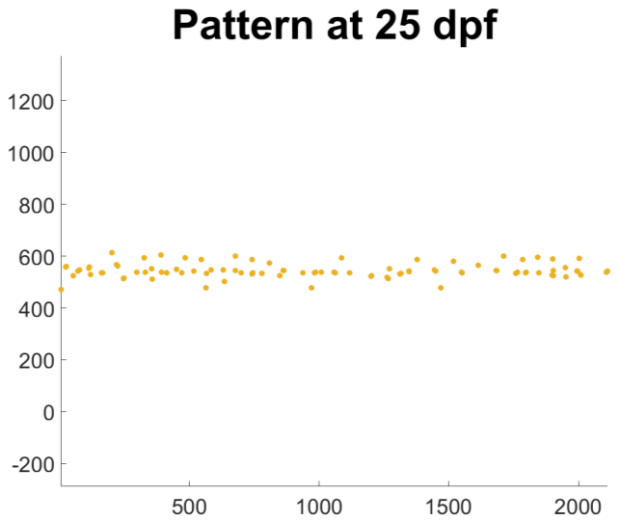
- Cell movement by differential equations

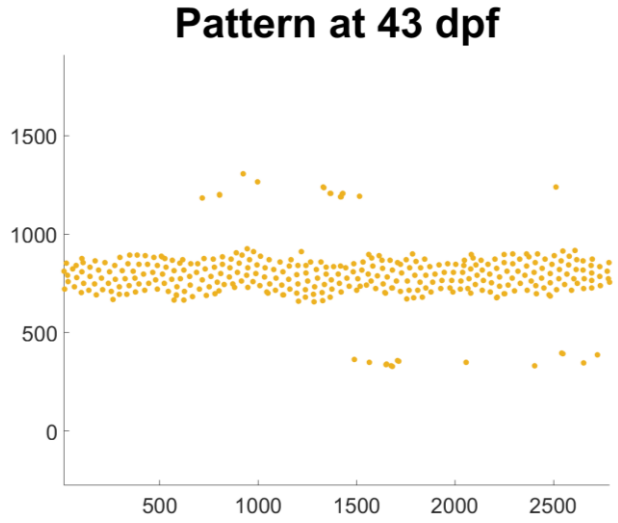
- Stochastic rules for other cell interactions

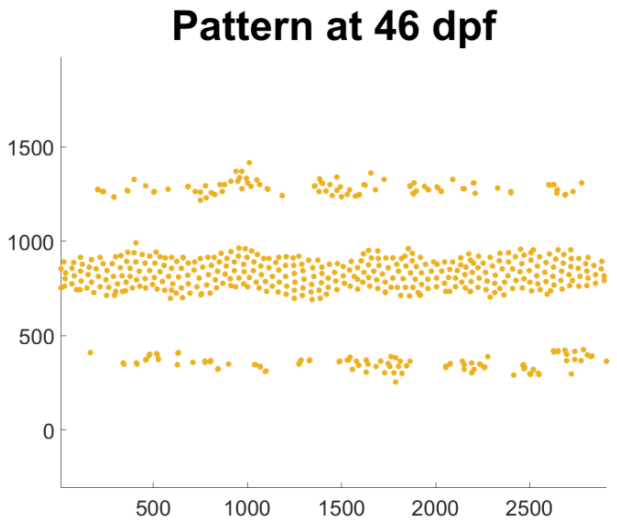


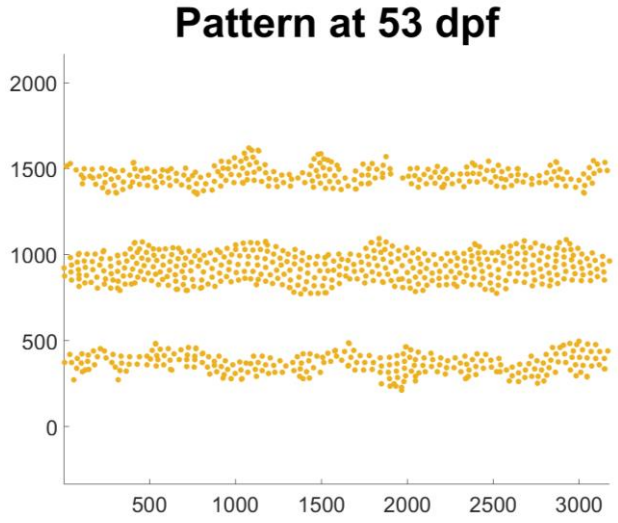
AGENT-BASED MODEL OF PIGMENT CELL INTERACTIONS

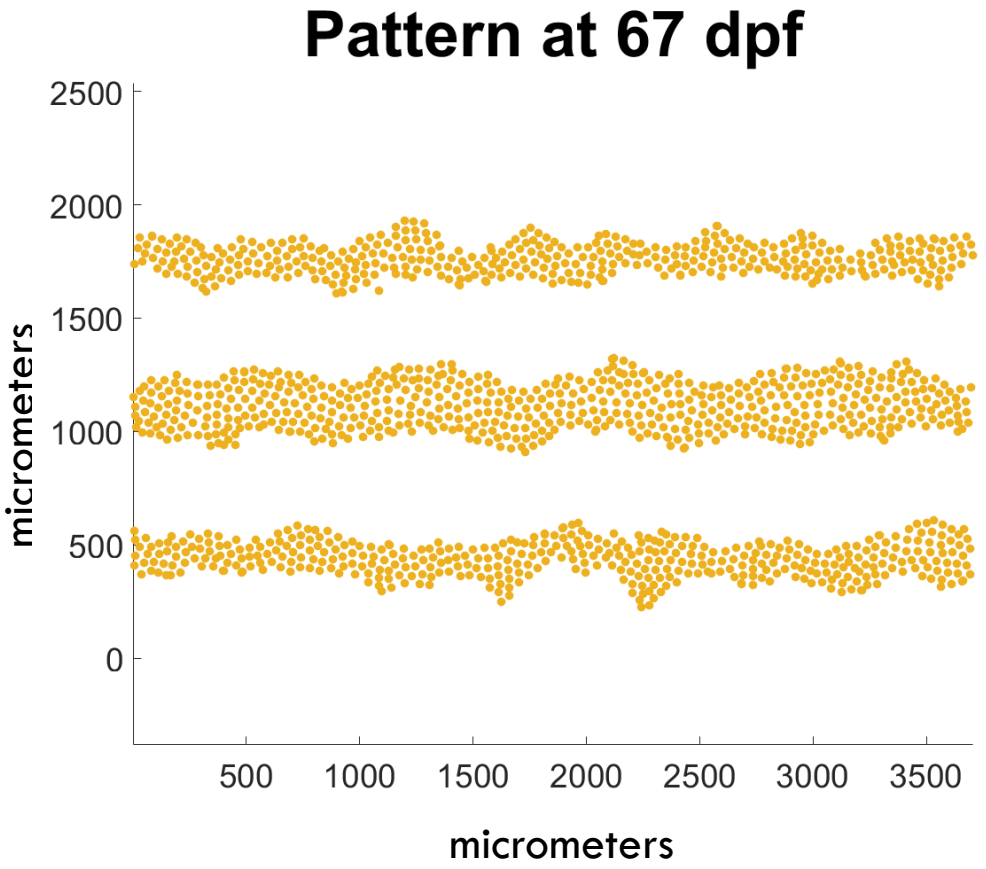
{Model: Iridophores as a source of robustness in zebrafish stripes and variability in Danio patterns, Volkening, Sandstede, *Nature Commun* 2018}









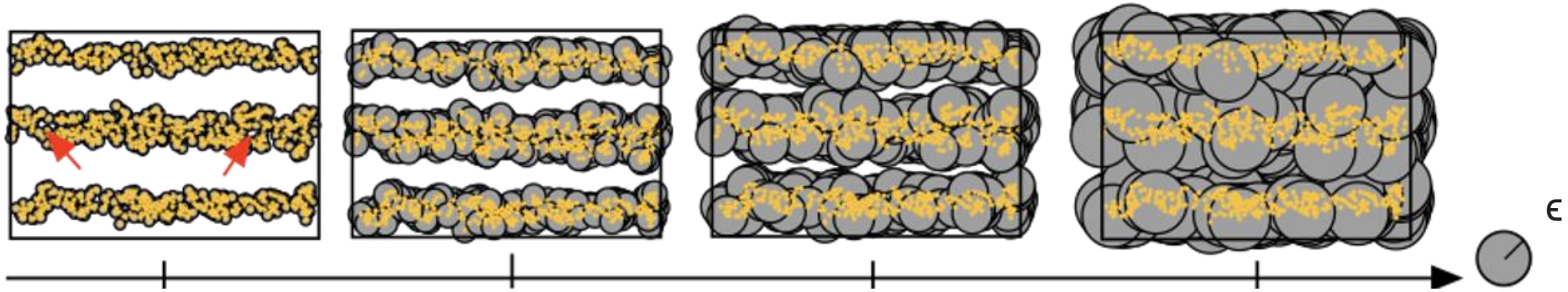


How many gold stripes are present at each time?

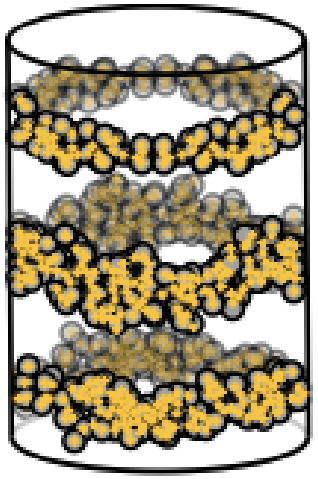
CHALLENGE: QUANTIFYING PATTERN FORMATION IN TIME

PRIOR WORK: PERSISTENT HOMOLOGY OF ZEBRAFISH

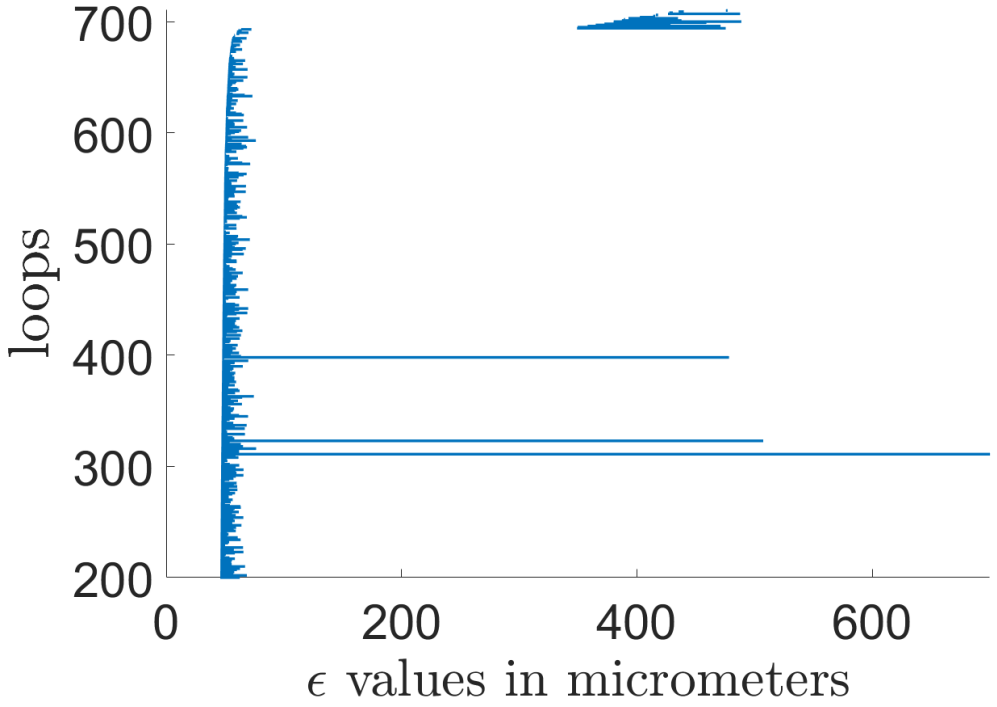
- Periodic domain



- Persistence = length of bar
- Loops with long bars are considered stripes

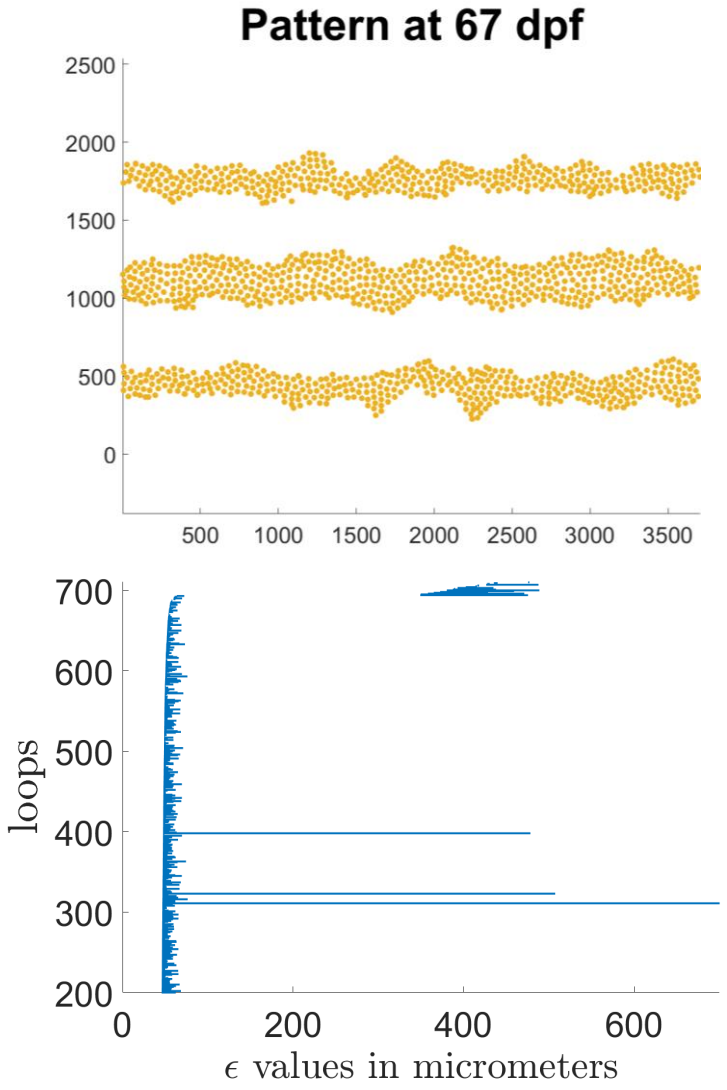


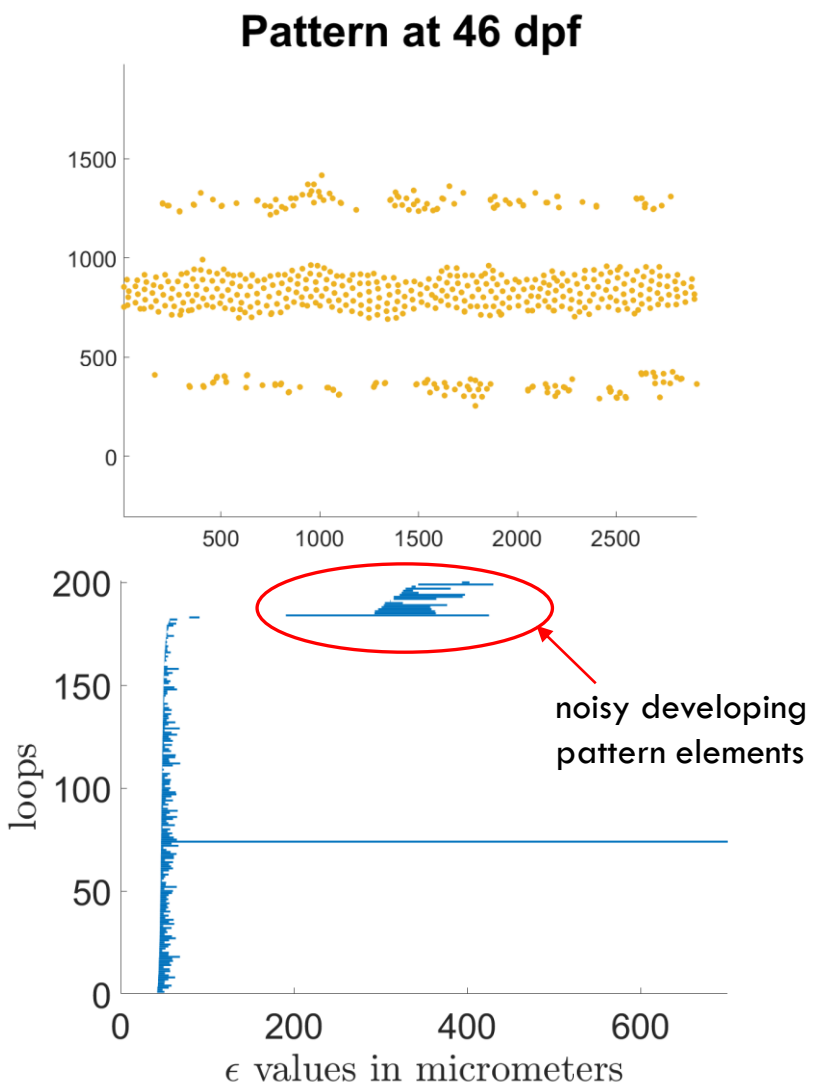
- McGuirl *et al.* used one persistence threshold: $T^1 = 200$ μm (specified *a priori*) to distinguish between noise and stripes



{Reference: Topological data analysis of zebrafish patterns, McGuirl, Volkening, Sandstede, *PNAS*, 2020}

- Challenge: not flexible or applicable to all timepoints in zebrafish development
- **How can we automatically choose a threshold that is dependent on the pattern alone?**

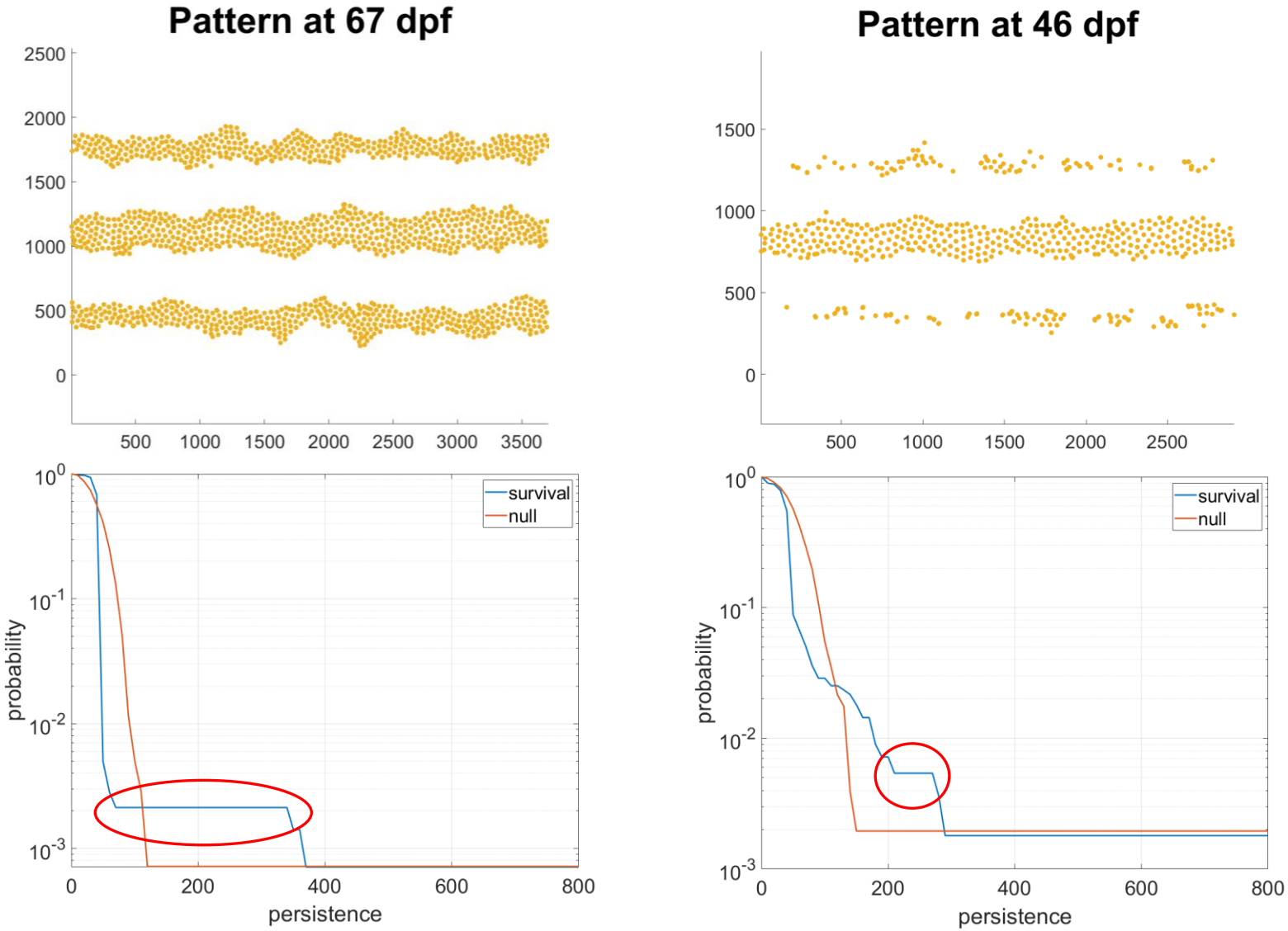




LIMITATIONS: DEPENDENT ON HYPERPARAMETERS AND DEVELOPED FOR FULLY FORMED PATTERNS

Ciocanel *et al.* used survival functions to identify meaningful loops in data on intracellular transport. We adapt this approach, and **use survival functions to identify persistence thresholds for fish patterns**

<u>Survival function S</u>:
S(p) is the probability of randomly choosing a loop with persistence greater than or equal to p, from the set of loops



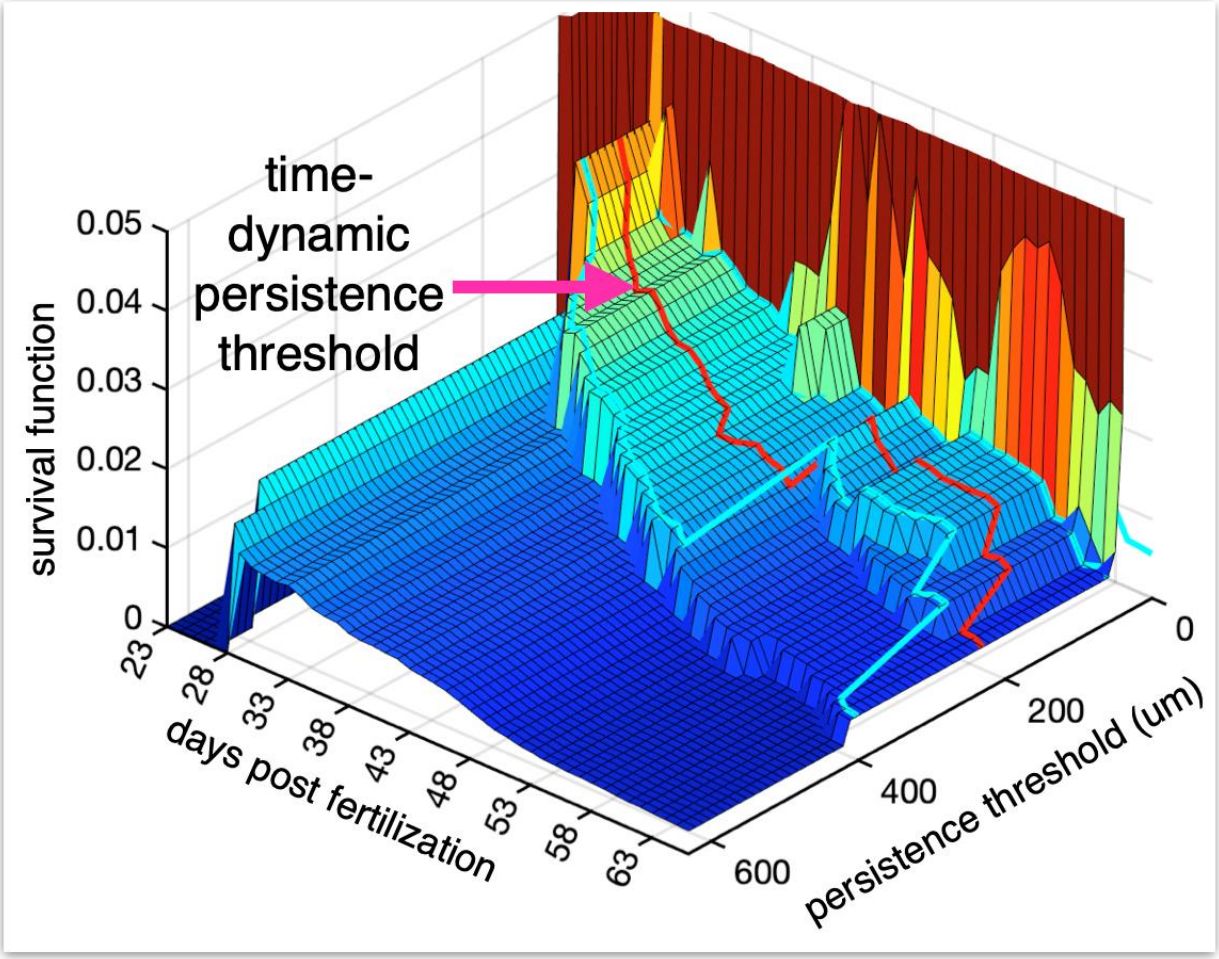
OUR APPROACH: APPLYING SURVIVAL FUNCTIONS

{Reference: Topological Data Analysis Approaches to Uncovering the Timing of Ring Structure Onset in Filamentous Networks, Ciocanel, Juenemann, Dawes, McKinley, *Bull Math Biol.*, 2021}

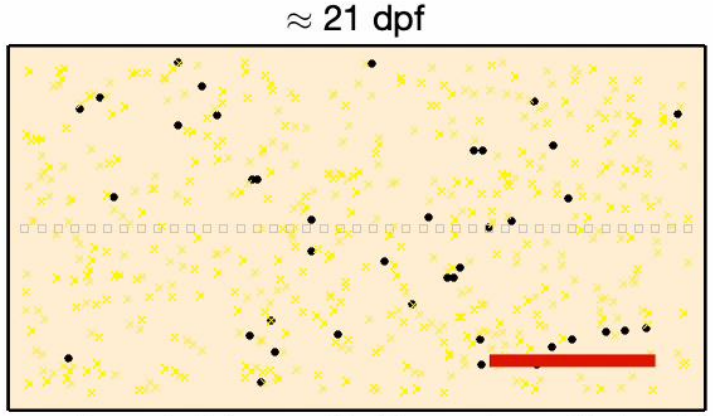
OUR APPROACH: SURVIVAL FUNCTIONS IN TIME

<u>Choosing a time-dependent theshold</u>:

- Identify first plateau (at least 30 µm wide) at each timepoint of development
- Persistence threshold is midpoint of plateau at each given time
- Full plateau width provides a measure of confidence in our threshold



- We specify persistence thresholds for loops by survival method
- Stripe width is based drops in gold and black stripe counts
- Curviness involves clustering based on stripe count
- Spots count uses dim 0 persistence, with a threshold depending on mean cell-to-cell distance

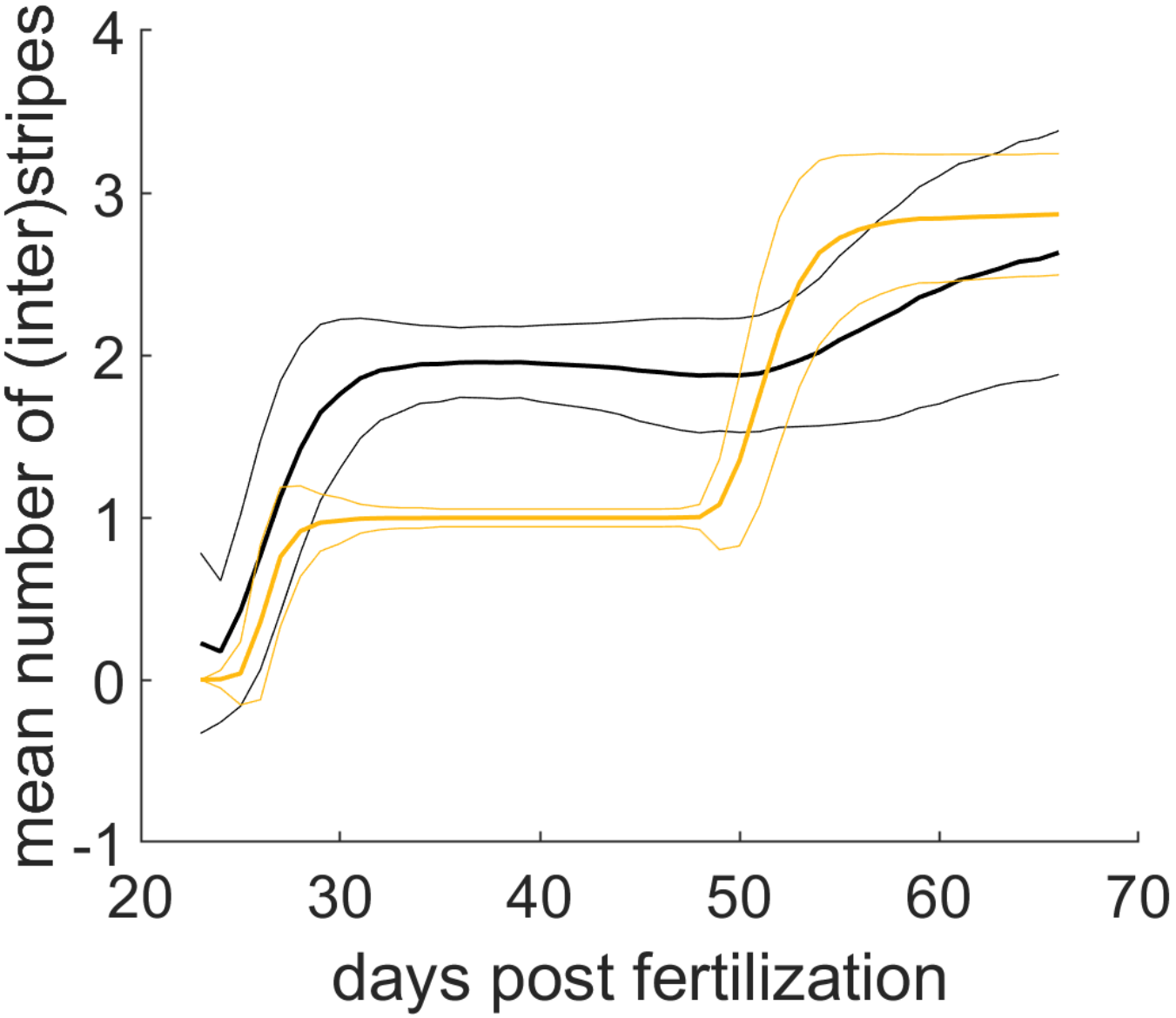


RESULTS: APPLYING OUR METHODS TO ZEBRAFISH

RESULTS

We ran statistical analyses on 1000 *in silico* patterns to understand large-scale behavior

- Black cell (melanophore) stats in black
- Gold cell (xanthophore) stats in gold



THANK YOU FOR LISTENING

Summary of method:

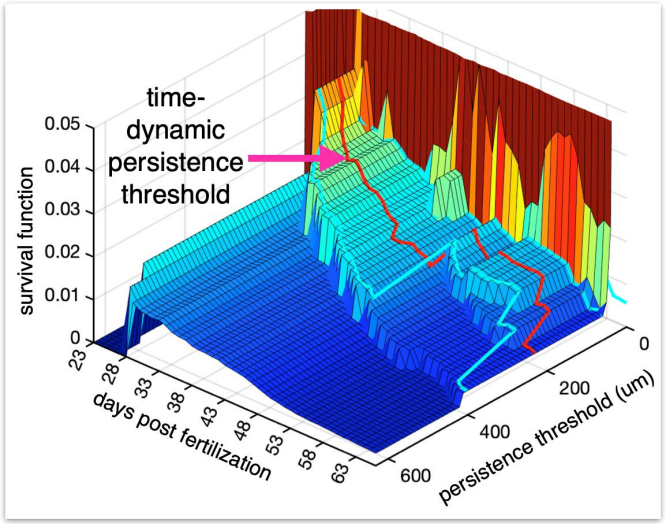
Survival function

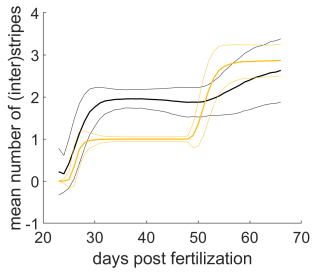
↓

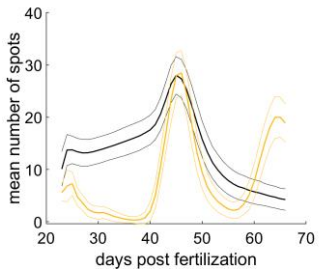
Persistence threshold

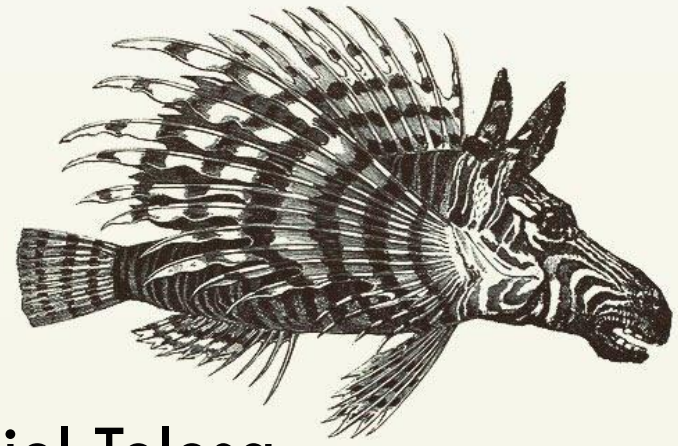
↓

Pattern quantification in time









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Ref: Tolosa, Volkening. In prep.

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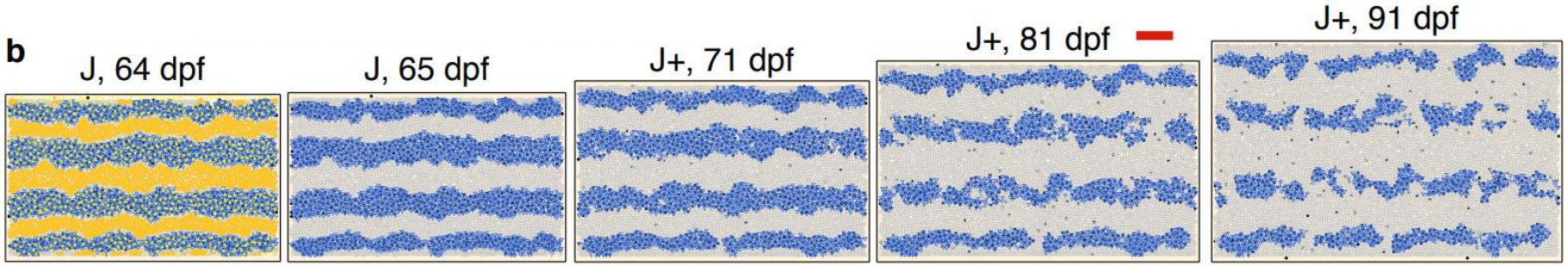
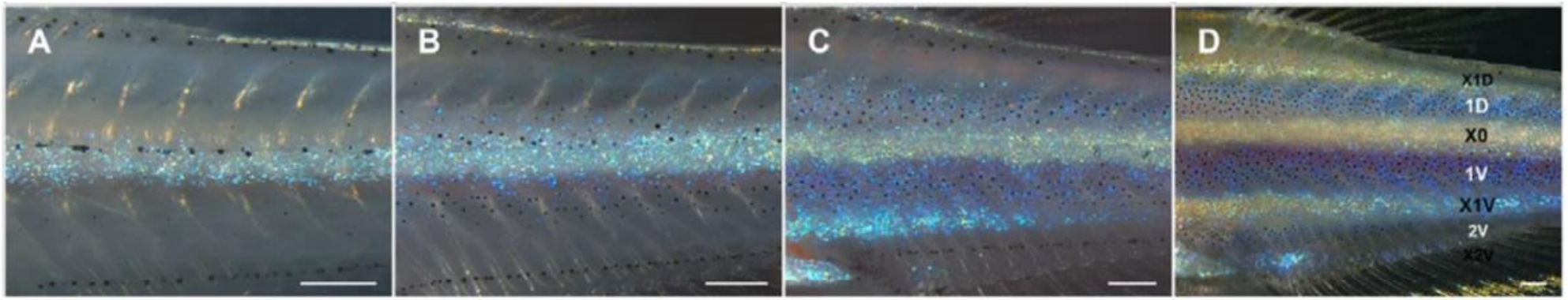
{Title: Zebrafish by Berliner Babylon, https://berlinerbabylon.com/.}

- Increasing the temperature of the environment can alter the striped pattern



- Apply out methods to *in vivo* data.



FUTURE WORK

{Figures: Iridophores as a source of robustness in zebrafish stripes and variability in Danio patterns, Volkening, Sandstede, *Nature Commun* 2018}