Geometric models for robust encoding of dynamical information into embryonic patterns [1]

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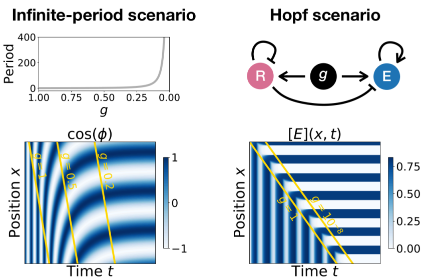
Introduction

Background:
Somites are the precursors of the vertebrae. They consist of groups of cells separated by boundaries that form one after the other. Somites are divided into anterior and posterior compartments.

Experimental evidence:
Initially, the concentration of proteins involved in somite formation oscillates in single cells. The oscillations slow down and eventually stop when a cell is incorporated into a somite. A cell ends up with either high or low concentration of the proteins depending on its position within the somite [2].

Objective:
Model such transition from a dynamic oscillatory regime to a static multistable regime within the framework of dynamical systems theory. Assess the robustness of different transition scenarios.

Previous theoretical work:
Two main approaches are currently used to model somite formation: the infinite-period scenario (phase models with period divergence [2]) and the Hopf scenario (gene networks undergoing a Hopf bifurcation [3]).



Model

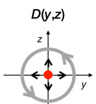
We use abstract, geometric variables *y* and *z* to represent the state of the system.

Initial dynamical regime *D(x,y)*: oscillations

Final dynamical regime *S(x,y)*: multistability

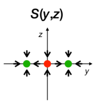
The transition from the initial to the final regime is controlled by parameter *g*:

$$\dot{P} = \theta_D(g)\, D(P) + \theta_S(g)\, S(P)$$



where *P*=(*y*,*z*) is a vector and the weights θ_D and θ_S are smooth functions of *g*.

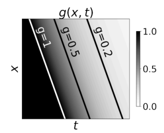
Such a smooth transition between two dynamical regimes could be achieved via the interplay between two enhancers [4]. An enhancer is a region of DNA on which proteins can bind to modify the transcription of a given gene.



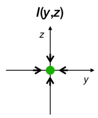
Results

The SNIC bifurcation is a potential mechanism (from a dynamical systems theory perspective) for the infinite-period scenario.

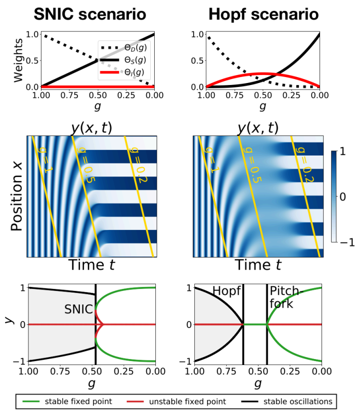
A linear transition leads to a SNIC bifurcation, during which the period of oscillations diverges.

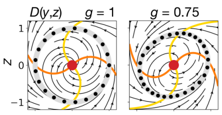


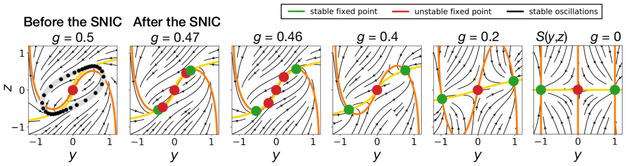
To get a Hopf bifurcation, we need to introduce an intermediate regime *I*(*P*) characterized by a single stable fixed point.



2D models allow us to visualise directly the flow in phase space.

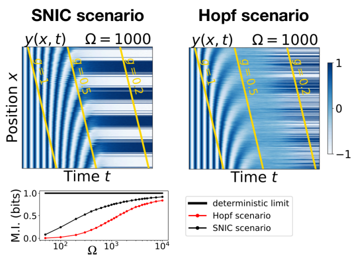






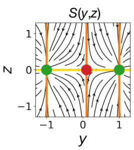
Pattern formation via a SNIC bifurcation is more robust to noise.

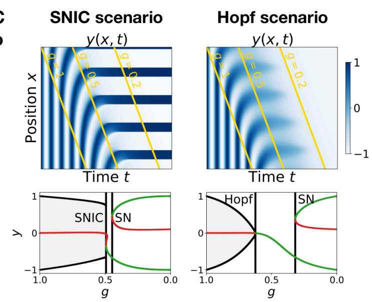
To quantify the robustness to noise, we use a metric based on the mutual information (M.I.): the higher the M.I., the more robust the model. Parameter Ω represents the level of noise: higher Ω corresponds to lower noise.



Pattern formation via a SNIC bifurcation is more robust to parameter changes.

We introduce an asymmetry in the basins of attraction of the two stable fixed points of the static regime.

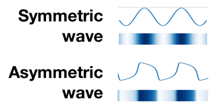


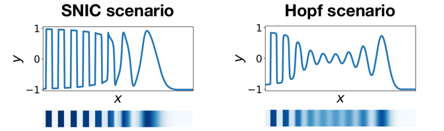


Discussion

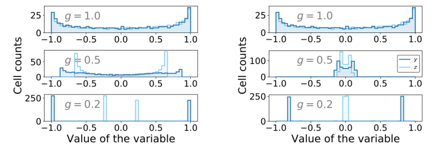
SNIC-based pattern formation is consistent with the latest experimental observations.

The spatial wave profile across the embryo is asymmetric, due to the relaxation-like oscillations near the SNIC bifurcation.



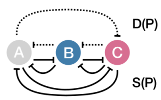


The distribution of state variables stays broad until cell-type specification.



The period of oscillations diverges at the bifurcation [5].

We confirmed all the results presented here with a similar model based on gene regulatory networks for the dynamic and static regimes.



References

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Acknowledgments

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