02

Modeling biological development with agent simulation

Estimating cellular interactions from patterns

Abstract

Self-organized multicellular patterns emerging from intercellular interactions are fundamental to diverse biological functions, such as detoxification in hepatic lobules and camouflage through stripe patterns in zebrafish skin. However, quantitatively inferring the underlying intercellular interactions that give rise to target multicellular patterns remains a challenging inverse problem. In this study, we propose a framework that estimates parameters governing adhesion and repulsive forces between cell types directly from target multicellular patterns. Our method extracts robust topological features across multiple spatial scales and employs a pretrained surrogate model to efficiently infer interaction parameters. We validate the framework using both simulated and image-based zebrafish pigment patterns. This framework provides an efficient and interpretable approach for linking multicellular pattern geometry to intercellular interactions and has potential applications in tissue engineering, including the design and control of organoid morphogenesis.

Multicellular Pattern Formation

Biological functions enabled by multicellular patterns

Representative multicellular patterns and associated functions

Liver: Detoxification

Hepatocytes, Endothelial cells, Kupffer cells, and etc…

Stripes patterns in zebrafish sides: Camouflage

Xanthophores and melanophores

Early larva　Mid larva　Adult

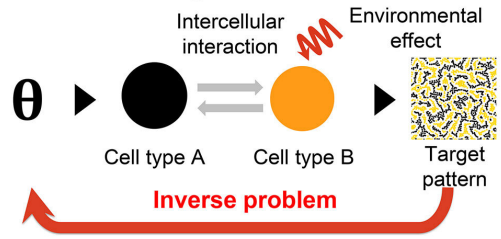
These patterns arise from intercellular interactions

Objective：Estimating intercellular interactions that enables target multicellular patterns

→Applying the method to tissue engineering such as Organoids

Proposed method

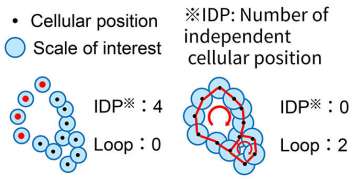
Estimate **parameters of intercellular interaction** from target multicellular patterns



θ: Parameters define adhesion and repulsive forces

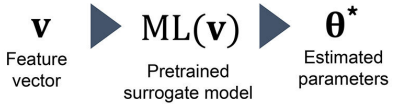
Topological features

Robust feature extraction by counting topological features at each scale.

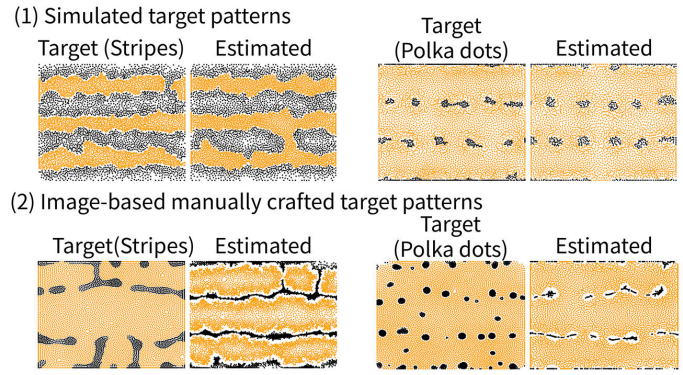


Inverse surrogate model

Efficient and direct estimation with surrogate modeling



Validation with zebrafish pigment formations



Result summary

Target pattern	Stripe	Polka-dots
(1) Simulated	○	○
(2) Image-based	△	△

○：Visually and quantitatively match

△：Roughly match, but there are some minor differences

(1) The framework successfully inferred intercellular interaction parameters from simulated target patterns.

(2) Minor discrepancies were found in image-based cases, but they could be used to refine the inverse surrogate model.

References

[1] A. K. Jin, K. Komiya, R. Nishikimi, K. Kashino, “Topology Informed Surrogate Modeling for Parameter Optimization in Multicellular Models,” *in Proc. International Conference on Biomedical and Health Informatics (BHI)*, 2025.

[2] K. Komiya, A. K. Jin, R. Nishikimi, K. Kashino, “Learning Pairwise Potential via Differentiable Recurrent Dynamics,” *in NeurIPS Workshop on Machine Learning and Physical Science*, 2025.

Contact

Kenji Komiya, Biomedical Informatics Research Group, Media Information Laboratory