Parallel Session

Mathematical Methods in Biology II

MODELLING HIERARCHICAL PATTERN FORMATION IN EPIDERMAL APPENDAGE DEVELOPMENT

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Keywords: Pattern formation, Reaction-diffusion, Chemotaxis, Mesenchymal self-organisation.

The periodic arrangement of hair follicles on the skin is initially determined during embryogenesis. Here, we propose a novel mathematical model that describes this process as an interaction of two distinct patterning mechanisms: a reaction-diffusion driven pre-pattern in the epidermis and mesenchymal self-aggregation in the dermis.

Both mechanisms are able to generate the same regularly inter-spaced dot pattern on their own. They have been extensively studied over the past decades - both from the experimental and the theoretical perspective. However, modelling approaches so far focused on just one of these two mechanisms. The molecular agents governing their interaction have only recently been identified. Glover *et al.* described a hierarchical mode of patterning in mice, where the reaction-diffusion driven pre-pattern in the epidermis governs the chemotactic self-assembly of dermal cells through TGFβ2 and FGF20 signalling [1].

Our hybrid model is based on these recent experimental findings. It combines the reaction-diffusion driven patterning in the epithelial layer with an agent-based mode of directed cellular motion underneath. We model the embryonal skin as a two-dimensional plane. Concentrations of the reaction-diffusion system in the epidermis and the chemoattractant secreted by the mesenchymal cells are modelled as partial differential equations and solved on a numerical grid. The discrete mesenchymal cells move in-between the grid points and interact with them to sense local concentrations and gradients. Furthermore, mechanical forces accounting for short-range repulsion are included. Both systems are coupled by adjusting the cells sensitivity to the chemoattractant gradient according to the local reaction-diffusion pattern.

Our simulations agree with experimental results and videos of mesenchymal cell aggregation. They show that this minimal model is sufficient to generate a regularly inter-spaced

dot pattern through the hierarchical interactions of epidermal and dermal patterning mechanisms. The reaction-diffusion pattern hereby limits cluster size of the underlying dermal self-aggregation and determines the location of these clusters. The model can also replicate the tendency of aggregates to rotate once they have assembled. Cluster rotation arises through the interaction of chemotaxis with mechanical inter-cellular forces. Our simulations show that the mean angular velocity of the cluster depends, among others, on the cell number and the shape of the chemoattractant gradient. We are currently working to expand the reaction-diffusion system from two components to include all relevant molecular entities. We also aim to recreate experimental conditions imposed on self-aggregating mesenchymal cells as described by [1] to further investigate the model's characteristics.

References

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PATTERN PRODUCTION THROUGH A CHIRAL CHASING MECHANISM

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Keywords: Animal pigmentation patterns, Cellular motion, Pattern formation, Reaction-diffusion equations, Chasing dynamics.

Recent experiments on zebrafish pigmentation suggests that their typical black and white striped skin pattern is made up of a number of interacting chromatophore families. Specifically, two of these cell families have been shown to interact through a nonlocal chasing mechanism, which has previously been modeled using integro-differential equations. We extend this framework to include the experimentally observed fact that the cells often exhibit chiral movement, in that the cells chase, and run away, at angles different to the line connecting their centers. This framework is simplified through the use of multiple small limits leading to a coupled set of partial differential equations which are amenable to Fourier analysis. This analysis results in the production of dispersion relations and necessary conditions for a patterning instability to occur. Beyond the theoretical development and the production of new pattern planiforms we are able to corroborate the experimental hypothesis that the global pigmentation patterns can be dependent on the chirality of the chromatophores.

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PATTERN FORMATION INDUCED BY DYNAMIC DEFORMATION OF DOMAIN

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Keywords: Pattern formation, Cellular and nuclear dynamics, Phase-field method.

Nuclear architecture (macro-scale pattern of chromatins), which plays an important role in organizing the function of the cell, is composed of heterochromatin and euchromatin regions. Conventional nuclear architecture where the heterochromatin is enriched in the periphery of the nucleus is the primary structure in the majority of eukaryotic cells, and the rod cells of diurnal mammals contain this structure. In contrast, inverted nuclear architecture where the heterochromatin is distributed in the center of the nucleus occurs in the rod cells of nocturnal mammals. Interestingly, the inverted architecture found in the rod cells of the adult mouse is formed through the reorganization of conventional architecture. However, the mechanism by which the nuclear architecture changes remains largely unknown. Here, we combined a new modeling approach using phase-field method and experiments of *in vitro* and *ex vivo*. We found that the deformation of nucleus via actomyosin contractility contributes to the driving force of genomic reorganization and can play a critical role in the process of chromatin pattern formation during differentiation [1].

References

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CELL ADHESION AND FLUID FLOW JOINTLY INITIATE BIOFILM SPATIAL STRUCTURE

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Keywords: Pattern formation, Correlation function, Bacterial biofilms, Stochastic modeling, Microbial ecology.

Biofilms are microbial collectives that occupy a diverse array of surfaces. The function and evolution of biofilms are strongly influenced by the spatial arrangement of different strains and species within them [1], but how spatiotemporal distributions of different genotypes in biofilm populations originate is still underexplored. In this presentation, I will present our recent work on the origins of biofilm genetic structure [2]. Combining model development, numerical simulations, and microfluidic experiments using the human pathogen *Vibrio cholerae*, and using spatial correlation functions to quantify the differences between emergent cell lineage segregation patterns, we find that strong adhesion often, but not always, maximizes the size of clonal cell clusters on flat surfaces. Counterintuitively, our model predicts that, under some conditions, investing in adhesion can reduce rather than increase clonal group size. Our results emphasize that a complex interaction of fluid flow and cell adhesiveness during surface colonization can underlie emergent patterns of biofilm genetic structure. This structure, in turn, has an outsize influence on how biofilm-dwelling populations function and evolve.

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