Physical Modeling of Growing Cellular Mosaic Patterns in Fish Retina

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2016.07.09 “Bigwave of Theoretical Science in Okinawa”
Cone Cellular Mosaic on Fish Retina


[T. Allison, website]

[OIST Developmental Neurobiology (Masai) Unit, website]
Vertebrate Eye and Retina

[Cone Cells:
- B
- UV
- R
- G

Figure: from Wikipedia]
Cone Cellular Mosaic on Fish Retina

Medaka-type

- p4mg

Zebrafish-type

- c2mm

[OIST Developmental Neurobiology (Masai) Unit, website]


Noriaki Ogawa
Outline

1. Cone cellular mosaic
2. Directionality of mosaic pattern
3. Modeling
4. Analysis of the model
5. Summary
Experimental/Observed Facts

Before the mosaic pattern formation:

(1) Differentiation is determined in advance. [Suzuki et. al, 2013]

(2) $G$ & $R$ make a bound state (double-cone).
Mosaic Generating Mechanism (?)

We can guess that:

(1) UV B R move around in CMZ

(2) Neighboring cells are bounded by binding proteins

Mosaic patterns realized as stable states (?)
Directionality of the mosaic pattern

Zebrafish-type

Rotated pattern

Info of direction?
Retinal Growth: Sketch

CMZ
(ciliary marginal zone)

Mosaic

25 \mu m

D. A. Cameron and S. S. Easter (1993)
Visual Neurosci. 10: 375-384
Directionality of the mosaic pattern

Noriaki Ogawa

Zebrafish-type

Rotated pattern

Our result

Growth

Info of direction?
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Neighbor-bonding Model (TMI model)
[Tohya-Mochizuki-Iwasa, 1999]

- B, UV or double-cone RG lives in a lattice site.

- Binding energy between neighbors:

\[ E = - \sum_{\langle i,j \rangle} \sigma_{ij} \]

- States are realized statistically:

\[ P \propto e^{-E/T} \]

( T: “effective temperature” )
Mosaic Pattern as a Stable State

Metropolis Simulation

(random initial state)
Mosaic Pattern as a Stable State

Metropolis Simulation

(50% : 50%)
Retinal Growth: Sketch

CMZ
(ciliary marginal zone)

Mosaic

25 µm

D. A. Cameron and S. S. Easter (1993)
Visual Neurosci. 10: 375-384
Modeling of Retinal Growth

front-end

New layer

“Pool” of new cone cells
Markovian Model

- 6 states per 1 cell: 6^w Configurations per line
- Previous layer determines the next statistically

Markov-chain system

Transition matrix \( T^i_j \) \( (= P(i \rightarrow j)) \):

\[
T^i_j = \frac{\exp(-E_{ij}/T)}{\sum_k \exp(-E_{ik}/T)}
\]

\( E_{ij} = -U_j - V_{ij} \)

Intra-layer bonding  Inter-layer
Stable Patterns at T=0

Wild-type (1)

Wild-type (2)

Rotated

Grow
T > 0: Can the rotated stripe exist?

One-shot example of simulation: \(( w = 16 , T=0.5)\)

"Rotated zebrafish" pattern

Dynamical transition process

Wild-type zebrafish pattern
T > 0: Can the rotated stripe exist?

One-shot example of simulation: \(( w = 16, T=0.5)\)

\{ "Rotated zebrafish" pattern \}

\{ Dynamical transition process \}

\{ Wild-type zebrafish pattern \}
Quantitative plot of transition

Agreement ratio with wild/rotated patterns at n-th layer

Initial state: rotated pattern

Initial state: random

Grow

T=0.25  T=0.35  T=0.5 (w = 16)
Transition matrix

\[ \hat{T} = \hat{T}_0 + \delta\hat{T}(T) \]

Fluctuation

<table>
<thead>
<tr>
<th>Wild-type</th>
<th>Rotated</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="matrix.png" alt="Matrix Image" /></td>
<td><img src="matrix.png" alt="Matrix Image" /></td>
</tr>
</tbody>
</table>

\[ \hat{T}_0 = \begin{pmatrix}
0 & 1 & 0 & 0 & \cdots \\
1 & 0 & 0 & 0 & \cdots \\
0 & 0 & 0 & \text{1} & \cdots \\
0 & 0 & \text{1} & 0 & \cdots \\
0 & 0 & 0 & 0 & \cdots \\
\cdots & \cdots & \cdots & \cdots & \cdots
\end{pmatrix} \]
### Eigen-spectrum of transition matrix

(w = 4, \(\beta=2\))

<table>
<thead>
<tr>
<th>(\lambda)</th>
<th>Wild-type pattern</th>
<th>Rotated pattern</th>
<th>(\omega = 4), (\beta=2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.2426 0.2426 0.2426 0.2426</td>
<td>0.0005 0.0005 0.0005 0.0005</td>
<td></td>
</tr>
<tr>
<td>-0.948</td>
<td>1 -1 1 -1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-0.948</td>
<td>1 -1 -1 -1</td>
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<tr>
<td>0.910</td>
<td>1 1 -1 -1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.865</td>
<td>-1 -1 -1 -1</td>
<td>0.8319 0.8076 0.8319 0.8076</td>
<td></td>
</tr>
<tr>
<td>0.864i</td>
<td>1 -0.97i -1 0.97i</td>
<td></td>
<td></td>
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<tr>
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<tr>
<td>-0.863</td>
<td>0.024 0.024 0.024 0.024</td>
<td>1 -0.971 1 -0.971</td>
<td>0.0764 0.014 0.0764 0.014</td>
</tr>
<tr>
<td>0.321</td>
<td>1 1 1 1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

...
Eigenvalues for $w \geq 8$

\[
\begin{align*}
\lambda_1 &= 1, \\
\lambda_{2,3} &= -1 + \mathcal{O}(g^3), \\
\lambda_4 &= 1 - \mathcal{O}(g^3), \\
\lambda_5 &= 1 - \mathcal{O}(g^2) \\
\lambda_{6,7} &= \pm \left(1 - \mathcal{O}(g^2)\right)i + \ldots \\
\lambda_8 &= -1 + \mathcal{O}(g^2) + \ldots \\
\end{align*}
\]

\[g \equiv e^{-1/T}\]}
Directionality of the mosaic pattern

Zebrafish-type

Rotated pattern

Our result

Growth

Info of direction?
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Summary

◆ Formation of retinal cone mosaic
  ✓ Cell moving & local binding
  ✓ Directionality: Why no rotated patterns??

◆ Modeling of cell binding & retinal growth
  ✓ Growth → Markov-chain system
  ✓ Wild-type pattern survives automatically!

◆ Prospects
  ✓ Comparison with experiments (KO, ...)
    → contribute to experimental study?
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Retinal Cone Mosaic

- How is the pattern generated?
- How is the fixed directionality realized?

Physical Modeling

Local bindings

Growth row-by-row

Markovian Growth Model

Transition matrix

Results

Simulation from rotated initial state

One-shot Example

Agreement ratio

Eigen spectrum of transition matrix

Wild-type Stripe

Rotated Stripe

Rotated stripes automatically break down & arrive at stable wild-type pattern!

Rotated stripes always correspond to smaller eigenvalues.