Coupling Hair Follicle Cycles to Produce Traveling Waves

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Examples of Biological Synchronization

- Pacemaker cells in the heart
- Discharging of brain cells during epileptic seizures
- Women’s menstrual cycles
- Hair growth in rodents – motivation for this study

Suzuki, et al.
The Hair Follicle Cycle

- Begins with catagen – apoptosis
- Telogen – rest, exogen usually occurs in this phase
- Anagen – growth, longest phase

www.keratin.com/aa/aa008.shtml
Objectives

- Simulate the hair follicle cycle with two models.
  - Activator/ inhibitor
  - Substrate/ depletion
- Create networks of follicle oscillators via different modes of coupling
  - To observe the effects of certain variables
  - To produce synchronization.
The Activator/Inhibitor Model

x – autocatalytic activator

y – inhibitor

\[
\frac{dx}{dt} = \frac{\varepsilon^2 + x^2}{1 + x^2} \cdot \frac{1}{1 + y} - ax
\]

\[
\frac{dy}{dt} = b - \frac{y}{1 + cx^2}
\]

Fall, et al.
The Substrate/Depletion Model

\[ \frac{dx}{dt} = \frac{v(y - x)(\varepsilon^2 + x^2)}{1 + x^2} - x \]

\[ \frac{dy}{dt} = k - x \]

x – product
y - reactant

Fall, et al.
Hopf Bifurcation

- Fixed point loses stability as the eigenvalues cross the imaginary axis of the complex plane
- Stable limit cycle
Perturbations and the Interaction Function (H)

\[
\frac{d\theta}{dt} = \frac{2\pi}{T_0} + \beta \sin(\omega t - \theta)
\]

\[\omega = \frac{2\pi}{T}\]

Phase difference between oscillator and stimulator

\[\phi = \omega t - \theta\]
Averaging

- \( Z(t) \) – response function
- \( G(x) \) – type of coupling
  - Diffusive coupling \( x' - x \)
  - Bath coupling \( f((x+0.01*x',y)-f(x,y))/0.01 \)
- \( H(\Phi) \) – interaction function; coupling as a function of phase difference between oscillators

\[
H_1(\phi) = \frac{1}{T} \int_0^T Z(t) \cdot G_1(X_0(t + \phi), X_0(t)) \, dt
\]
Diffusive coupling function via the activator

\[ H(\phi) = 17 + 12 \cos \theta - 18 \cos 2\theta - 11 \cos 3\theta + 31 \sin \theta + 16 \sin 2\theta - 3 \sin 3\theta \]

Diffusive coupling function via the inhibitor

\[ H(\phi) = 4 - 2 \cos \theta - 2 \cos 2\theta + 26 \sin \theta + 5 \sin 2\theta + \sin 3\theta \]
Network Equation

- 20 oscillators in the network
- Optional gradient ($\epsilon$)
- Coupling strength ($a$) – must be weak

\[ x_1 = 1 + ah(x_2 - x_1) \]
\[ x_{2..19} = 1 - \frac{(j-1)\epsilon}{20} + a(h(x_{j-1} - x_j) + h(x_{j+1} - x_j)) \]
\[ x_{20} = 1 - \frac{19\epsilon}{20} + ah(x_{19} - x_{20}) \]
1-D Arrays

- Kind of coupling
  - Via x or y variable
  - Via diffusive or bath coupling
- Coupling constant \( (a) \)
- Diffusion limit (number of neighbors)
- Heterogeneity \( (\varepsilon) \)

\[
x_{2,19} = 1 - \frac{(j-1)\varepsilon}{20} + a(h(x_{j-1} - x_j) + h(x_{j+1} - x_j))
\]
Types of Coupling ($\epsilon = 0, 2$ nearest neighbors)

- **Activator**
  - Diffusive Coupling
    - $a = 1$
  - Bath Coupling
    - $a = 5$

- **Inhibitor**
  - Diffusive Coupling
    - $a = 1$
  - Bath Coupling
    - $a = 5$

Sine component is too small
Coupling Constant ($\varepsilon = 0$, 2 nearest neighbors, diffusive coupling)

Activator

Inhibitor
Diffusion Limit (a = 1, ε = 0, diffusive coupling via activator)

2 neighbors

4 neighbors

6 neighbors
Introducing Heterogeneity (a = 1, diffusive)

eps = -1

eps = 1

eps = 5

Activator

2 nearest neighbors

Inhibitor

4 nearest neighbors

( same phenomena for 6 neighbors)
2-D Arrays

- Using Fourier approximation
- Simulates actual traveling waves in the mouse

Suzuki, et al.
2-D Arrays

Activator

Inhibitor

Diffusive

Bath
Types of Coupling ($a=1$, $\epsilon=0$, 2 nearest neighbor)

- **Diffusive coupling**
- **Bath coupling**
Adding a gradient induces synchronization for bath coupling via product

\[ \text{eps} = 0 \quad \text{eps} = 1 \quad \text{eps} = 5 \]
Diffusive coupling via

Product

Reactant

Bath coupling did not produce any patterns.
Results Summary – Types of Coupling

- Only 4 networks synchronized for both 1 and 2 D arrays.

<table>
<thead>
<tr>
<th>AI Model</th>
<th>1-D Array</th>
<th>2-D Array</th>
<th>SD Model</th>
<th>1-D Array</th>
<th>2-D Array</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diffusive</td>
<td>Activator</td>
<td>*</td>
<td>*</td>
<td>Product</td>
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<td></td>
<td>Inhibitor</td>
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</tbody>
</table>
Results Summary - Variables

1-D Arrays
- The only coupling mode which never synchronized was bath coupling via the reactant.
- Changing the gradient can induce traveling waves, reverse wave direction and produce synchrony.
- The coupling constant and the diffusion limit are proportional to synchronization speed.
- 4 nearest neighbor coupling can initially produce unusual patterns.

2-D Arrays
Conclusions

- The hair follicle cycle could be represented by either model.
- Most likely networks are those which synchronize for 1 and 2 D networks.
  - Diffusive coupling via activator, product, and reactant
  - Bath coupling via activator
Who cares??
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References