# Coupling Hair Follicle Cycles to Produce Traveling Waves

Megan Jeans [1,2]

[1] Bioengineering and Bioinformatics Summer Institute, Department of Computational Biology, University of Pittsburgh, PA 15261
2 Department of Bioengineering, Rice University, Houston, TX 77005

## Abstract

The hair follicle is a regenerative organ which oscillates among periods of growth, apoptosis, and dormancy. Although these cycles usually occur independently, they are clearly regulated by external factors and have been observed to synchronize in certain mutant rodents. Two common biochemical oscillator models were used to approximate the hair follicle cycle, the activator/ inhibitor model and the substrate /depletion model. The coupling function was calculated for several different modes of coupling to produce simulations of the one and two dimensional networking of hair follicles. Within these networks, the variation of relevant parameters produced traveling waves for both models and revealed interesting patterns based on the type and intensity of follicle communication. Ideally, this data will provide insight into the type of networking that really occurs in the mutant rodents.

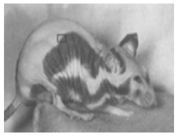


Figure 1. Mutant $Fox^{tw}$ mouse with traveling waves of pigmentation

Suzuki, *et. al*.

## Introduction

### Hair Follicle Cycle

Catagen - apoptosis
Telogen – resting
Anagen – growth


Figure 2. Three phases of follicle cycle

www.keratin.com/aa/aa008.shtml

### Modes of Coupling (G)

H(Φ)= sin(Φ)
Diffusive coupling – x'-x
Bath coupling-
(f(x+0.01*x',y)-f(x,y))/0.01

### Method of Averaging

H(t) – coupling function
Z(t) – response function
G(x) – type of coupling

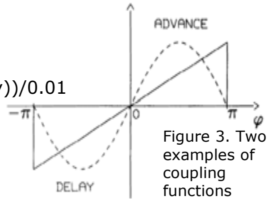



Figure 3. Two examples of coupling functions

Ermentrout & Rinzel

$$H_1(\phi) = \frac{1}{T}\int_0^T Z(t)\cdot G_1(X_0(t+\phi), X_0(t))\, dt$$

## Methods

It has been suggested by Paus and Foitzik that the hair follicle cycle mimics the chemistry of the cell cycle. Thus, two oscillatory models of the cell cycle were used to model the regenerative progress of the hair follicle.

### Activator/Inhibitor

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

$$\tau\frac{dy}{dt} = b - \frac{y}{1+cx^2}$$

Fall, *et al.*

### Substrate/Depletion

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

$$dy/dt = k - x$$

The optimal interaction function H(x) was calculated through the method of averaging and approximated using Fourier analysis.

Using their respective H(x), both models were coupled through various modes to produce 1-D arrays.

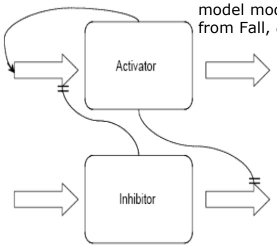



Figure 4. Activator/Inhibitor model modified from Fall, *et. al*

$$x_1 = 1 + ah(x_2 - x_1)$$

$$x_{2..19} = 1 - \frac{(j-1)\varepsilon}{20} + a(h(x_{j-1}-x_j) + h(x_{j+1}-x_j))$$

$$x_{20} = 1 - \frac{19\varepsilon}{20} + ah(x_{19} - x_{20})$$

$x_j$ = phase of the jth follicle

a = coupling constant - strength of coupling

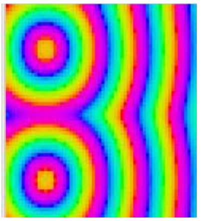
ε = gradient – hair follicles may have different natural frequencies

## Results

Four variables were examined:

1) Type of coupling: Only bath coupling via the y variable never synchronized under any conditions.
2) Coupling constant: found to be directly proportional to speed of synchronization.
3) Extent of coupling: directly proportional to speed of synchronization.
4) Gradient: can produce traveling waves and synchrony. Its variance can cause wave reversal.

Figure 5. 2-D array produced using Fourier approximation of bath coupling via the activator



| | AI Model | 1-D Array | 2-D Array | SD Model | 1-D Array | 2-D Array |
|---|---|---|---|---|---|---|
| Diffusive | Activator | * | * | Product | * | * |
| | Inhibitor | * | | Reactant | * | * |
| Bath | Activator | * | * | Product | * | |
| | Inhibitor | | | Reactant | | |

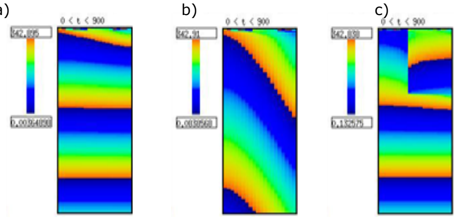



Figure 6. Various modes of diffusive coupling via the activator. a) no gradient, 2 nearest neighbors, b) gradient, 2 nearest neighbors, c) no gradient, 4 nearest neighbors

## 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
- Much left to be discovered about the biochemistry governing the cell cycles.

## Acknowledgements

Dr. G. Bard Ermentrout, Advisor
BBSI, University of Pittsburgh
NIH, NSF

## References

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