Reaction Diffusion Mechanisms for Cell Condensation During Avian Limb Development

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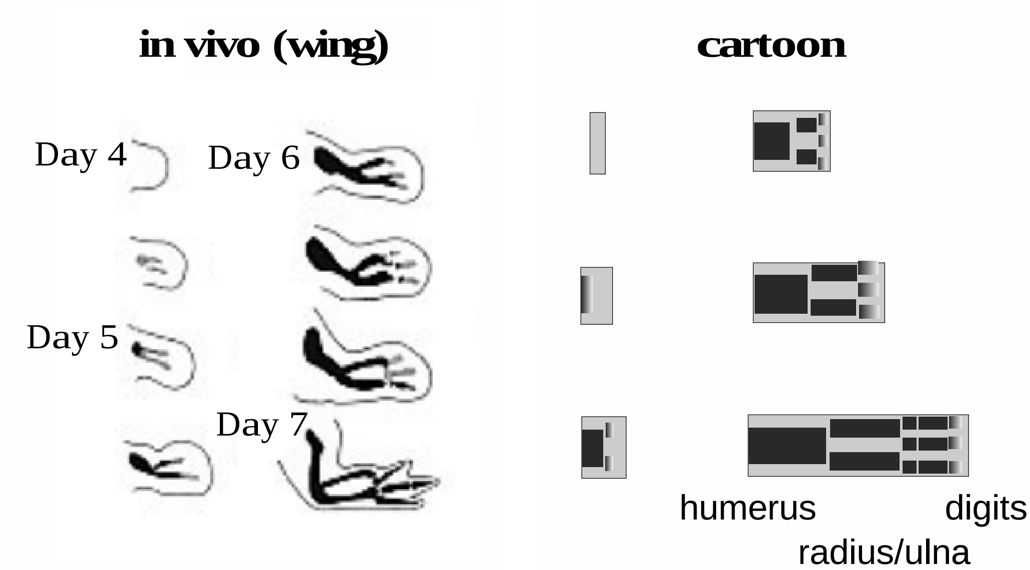
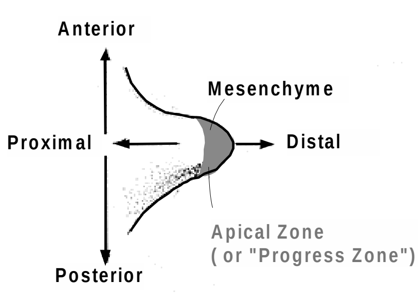
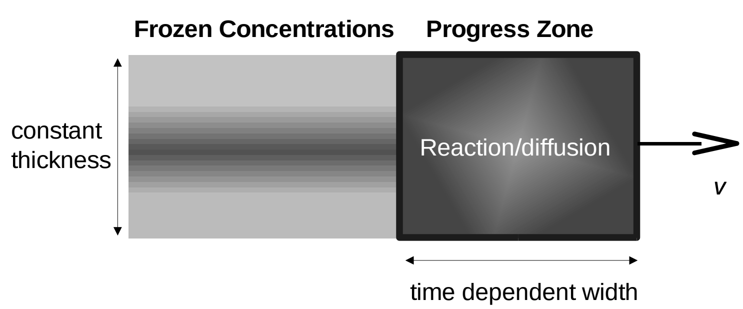
The Model

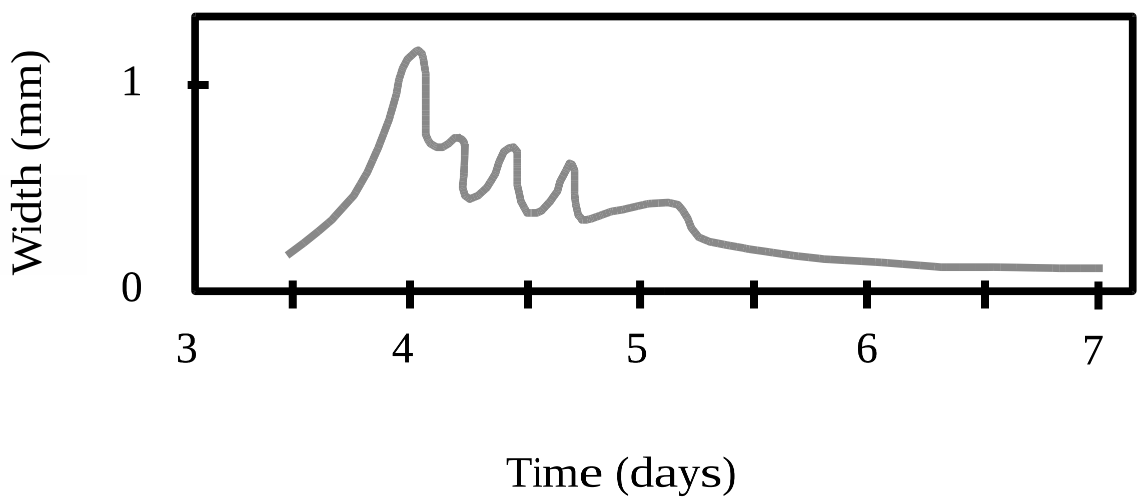
Newman and Frisch [1979]: Formation of skeletal pattern of chick limb by means of a reaction diffusion mechanism







The geometry of the Apical Zone varies with time. This may “steer” the pattern formation.



Changes in size of tip of chick wing during time of skeletal pattern formation. (from Newman, Frisch & Percus [1988])

Turing mechanism on a rectangle

$$\frac{\partial c_a}{\partial t} = r_a\left(c_a, c_i\right) + D_a \cdot \nabla^2 c_a$$
$$\frac{\partial c_i}{\partial t} = r_i\left(c_a, c_i\right) + D_i \cdot \nabla^2 c_i$$

- c_a, c_i: concentrations, r_a, r_i: reaction terms, D_a, D_i: diffusion coefficients
- Linearization close to equilibrium:

  $$r_a(\bar{c}_a, \bar{c}_i) = 0, r_i(\bar{c}_a, \bar{c}_i) = 0$$

  get

$$\frac{\partial}{\partial t}\mathbf{U} = A_0\mathbf{U} + D\nabla^2\mathbf{U}$$

- $D = \text{diag}\left(D_a, D_i\right)$, $A_0 = \text{Jac}(r)_{(\bar{c}_a, \bar{c}_i)}$, $\mathbf{U} = \left(c_a - \bar{c}_a, c_i - \bar{c}_i\right)^T$.

- von Neumann (no flux) boundary conditions

- **Solution**

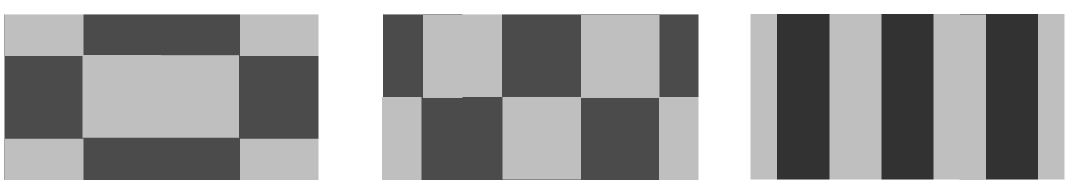
  $\mathbf{U}^i_{m,n}(x,y,t) =$

  $$\alpha^i_{m,n} \cdot \exp\left(\sigma^i_{m,n} t\right) \cdot \cos\left(q_{x,m} x\right) \cdot \cos\left(q_{y,n} y\right)$$

  for $m, n = 0, 1, 2, \ldots,\ i = 1, 2,$ where

  - $q_{x,m} = \frac{m\pi}{L_x}$, $q_{y,n} = \frac{n\pi}{L_y}$
  - $\sigma^i_{m,n}$ are the eigenvalues of $A - \left(q^2_{x,m} + q^2_{y,n}\right) D$ with eigenvectors $\alpha^i_{m,n}$

- Contour plot of components of $\mathbf{U}^i_{m,n}$



(2,2) (4,1) (6,0) ...

Biochemistry of Precartilage Condensation

extracellular matrix molecule **fibronectin**:

- early mediator of the condensation of mesenchymal cells
- makes cells more ”sticky”

family of **Transforming Growth Factor-βs** (TGF-βs):

- stimulate own synthesis and the production of fibronectin
- possible **activator** morphogen in a Turing type reaction-diffusion process

corresponding **inhibitor**: not definitely identified

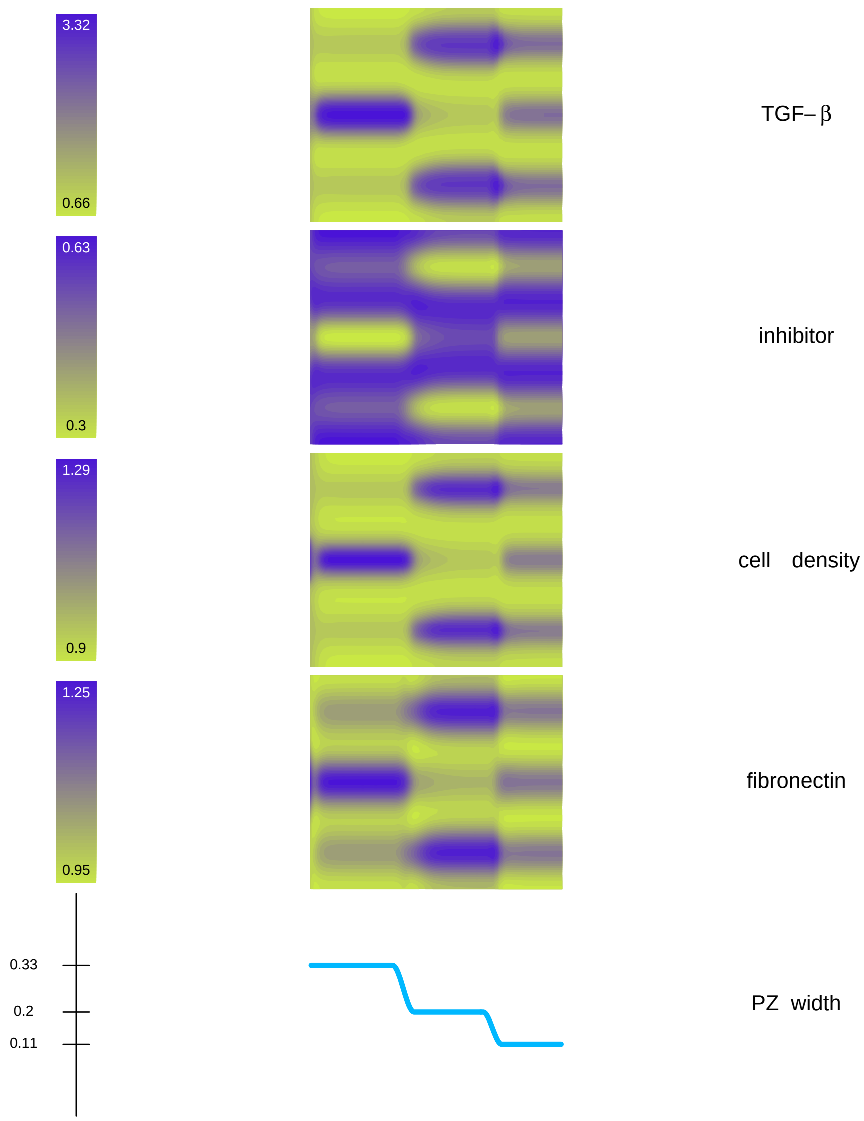
- possible connection to Ectodermal Fibroblast Growth Factors (FGFs) (Moftah et al., 2002)

The full model

$$\frac{\partial}{\partial t}c_a = f_a(c_a, c_i) + J_a(R) + D_a\nabla^2 c_a$$
$$\frac{\partial}{\partial t}c_i = f_i(c_a, c_i) + D_i\nabla^2 c_i$$
$$\frac{\partial}{\partial t}\rho = f_\rho(\rho, R, c_a) + D_\rho\nabla^2 \rho$$
$$\frac{\partial}{\partial t}R = f_R(R) - \chi\nabla\cdot(R\nabla\rho) + D_R\nabla^2 R$$

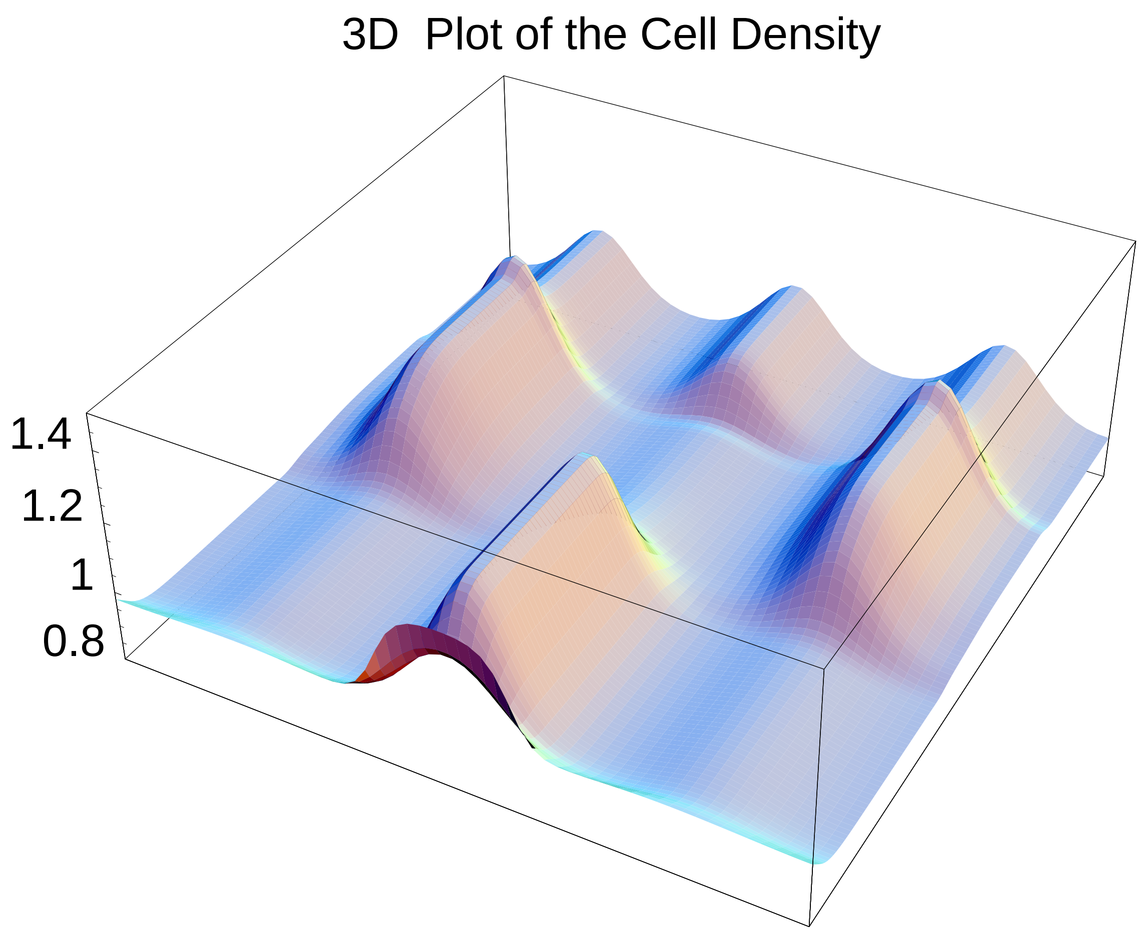
- c_a ... TGF-β concentration
- c_i ... inhibitor concentration
- ρ ... fibronectin concentration
- R ... cell density

Example 1: Full Model

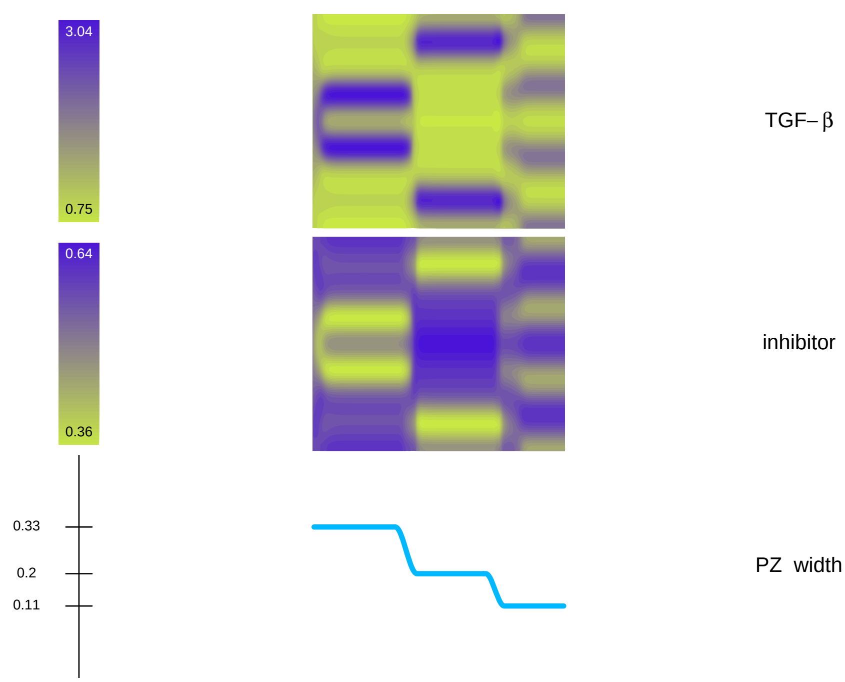


$$(2,2) \rightarrow (4,1) \rightarrow (6,0)$$

Full Model: Cell Density



Example 2: Only Activator-Inhibitor



Conclusions

- Mechanism can produce bifurcations.
- Inclusion of fibronectin makes process more stable.

Plans

- more realistic parameters
- effects of shape of domain