"Beyond Wave-Pinning; Dynamical Mechanisms for Cell Polarity and Interdigitation."

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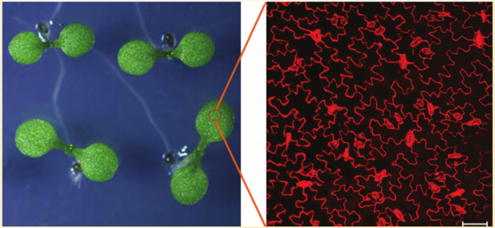
Pavement cells: Understanding the puzzle.

Jigsaw-like pattern in pavement cells



Reproduced from [Lin et al. 2014]. Cotyledon of Arabidopsis Thaliana. Scale bar 50[μm]

Factors

- Turgor Pressure.
- Pressure of Adjacent cells.
- Concentration of Rho-proteins of Plants (ROPs).

Cell Polarisation induced by a spatial gradient.

Cell Polarisation

The ability of a cell to form a front and a back, establishing a polarisation axis.

Studied in.

- *Budding yeast*
- Amoeba (*Dictyostelium discoideum*)
- Fibroblasts
- white blood cells
- nerve cells.

Role of Cell Polarisation.

is a primary step in...

- Motility.
- Cell Differentiation.

Disruption of cell polarity is a hallmark of cancer

Modelling: Reaction-Diffusion systems.

Polarised profile.

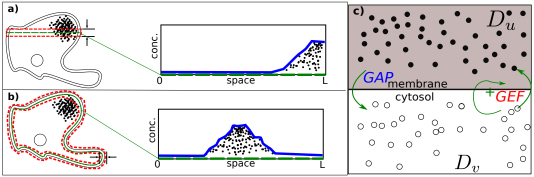
Any non-homogeneous stable spatial concentration profile of proteins and other factors.

Minimal approach.

- One Rho-Protein. $u(v)$ active(inactive).
- $D_u \ll D_v$

$$\partial_t u = D_u \partial_{xx} u + f(u, v)$$

$$\partial_t v = D_v \partial_{xx} v + g(u, v)$$



Modelling: Reaction-Diffusion systems, Wave Mechanism.

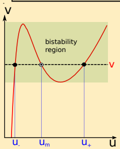
Wave-Pinning mechanism [Mori et al. 2008].

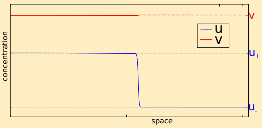
Alternative to Turing instability

$$\partial_t u = D_u \partial_{xx} u + f(u,v) \quad Du \ll D_v,$$

$$\partial_t v = D_v \partial_{xx} v - f(u,v),\ T = \int u + v$$

$$f(u,v) = \gamma \frac{u^2 v}{K^2 + u^2} - \eta u + \delta v$$



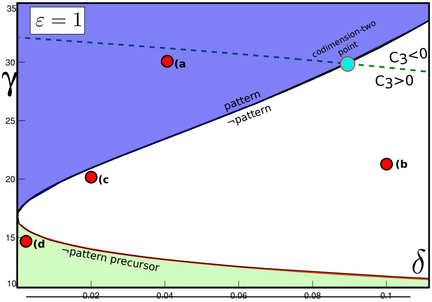


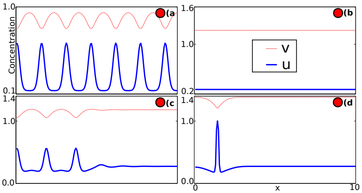
General Model[1]: source and loss terms

$$\text{(1a)} \qquad \partial_t u = \delta \partial_{xx} u + F(u,v) - \varepsilon\theta u,$$

$$\text{(1b)} \qquad \partial_t v = \partial_{xx} v - F(u,v) + \varepsilon\alpha,$$

$$F(u,v) = \left(\gamma \frac{u^2 v}{1+u^2} - \eta u + v\right) \qquad x \in [0,\mathcal{L}]\,.$$

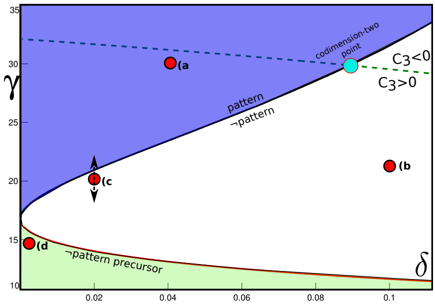




δ	γ	η	ε	θ	α
[0,0.2]	[15,40]	5.2	1	5.5	1.5

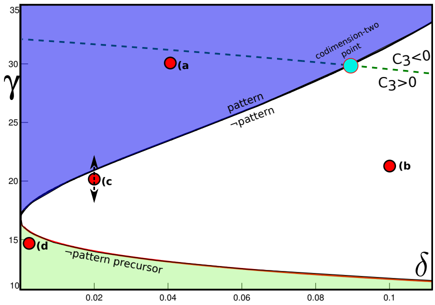
[1] Inspired by [Breña-Medina et al PRE 2014]

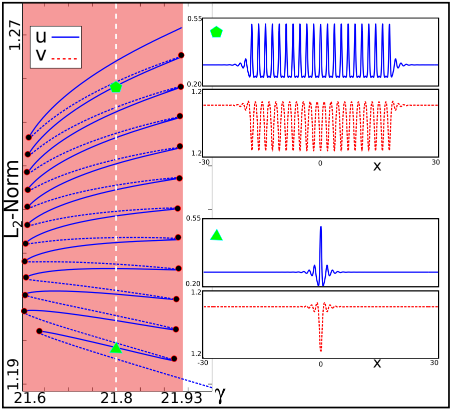
1-Parameter continuation of Localised Structures (AUTO) ($\varepsilon = 1$).



Prototype model for cell polarisation.

1-Parameter continuation of Localised Structures (AUTO) ($\varepsilon = 1$).





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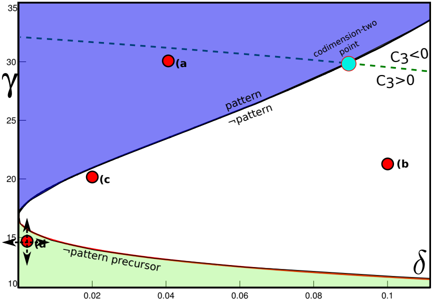

Prototype model for cell polarisation.

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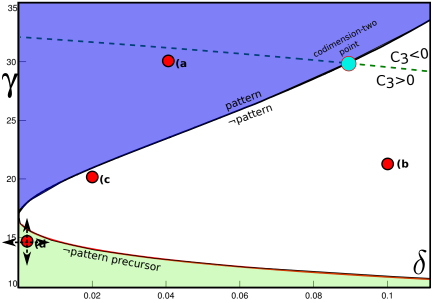
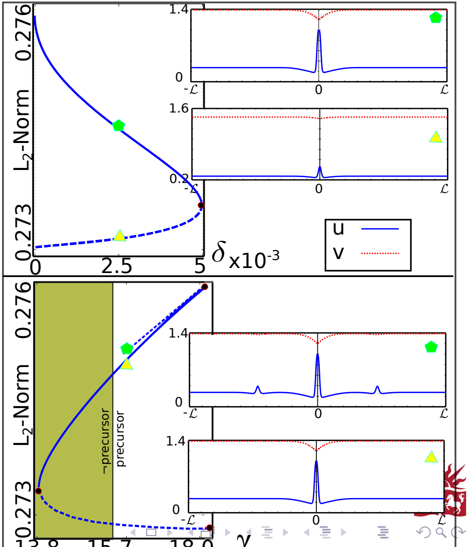
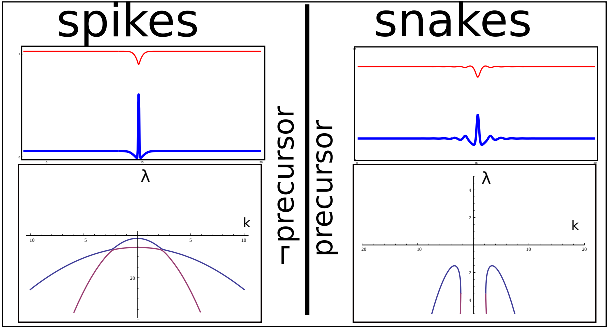


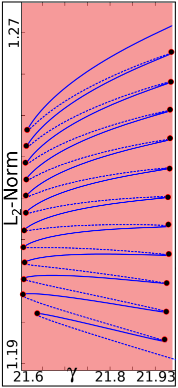


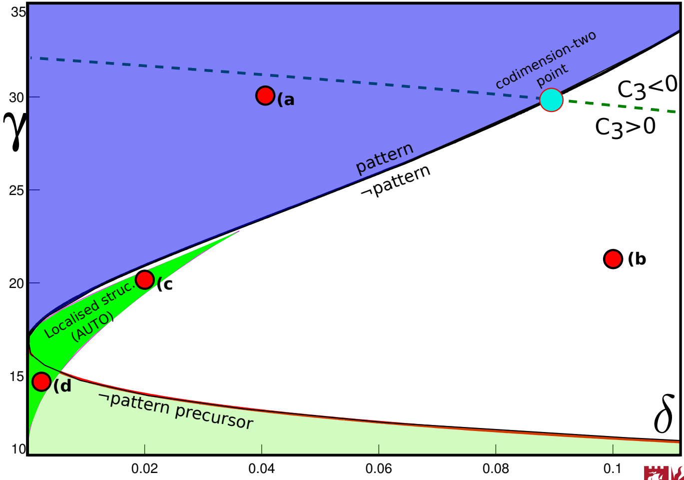
First Result.

Numerically we have found a transition between the two localised structures ubiquitous in P.D.E.
This transition seems to be characterised by the transition in the eigenvalues of the homogeneous state

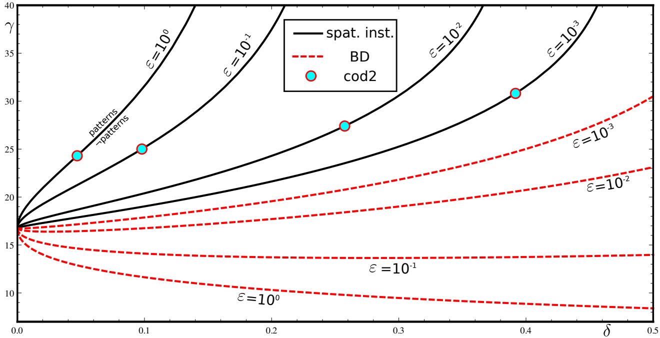


2-Parameter continuation of Localised Structures.



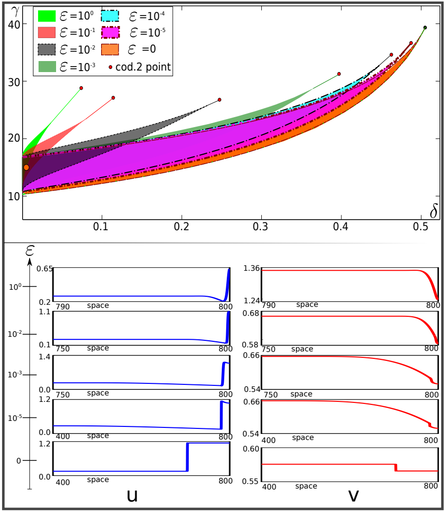


Limit $\varepsilon \to 0$: From localised structures to fronts.



The equivalent to the front is the spike solution.

Limit $\varepsilon \to 0$, 2-Parameter continuation of Localised Structures.



Front region($\varepsilon = 0$)

$$(2) \quad 0 = \delta \partial_{xx} u + f(u, v)$$

$$(3) \quad 0 = \partial_{xx} v - f(u, v)$$

(2)+(3), (2)-(3)

$$R = \delta u + v, \; S = \delta u - v.$$

B.V.P.

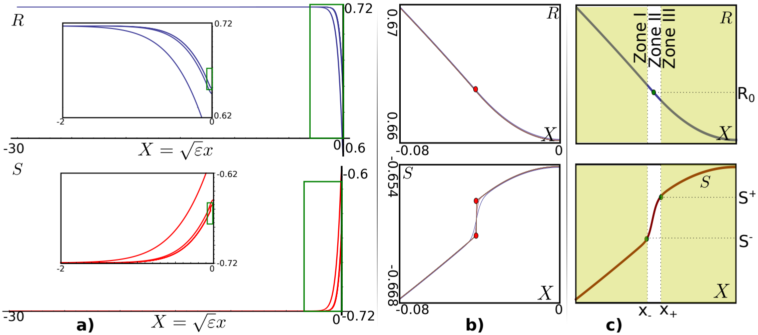
$$\partial_{xx} R = 0$$

$$\boxed{\partial_{xx} S = -2f(S, R_0)}$$

Matched Asymptotics.

Introducing the change of variables:

$$u = \frac{(R+S)}{2\delta}, v = \frac{R-S}{2} + \varepsilon\beta_1, X = \sqrt{\varepsilon}x, \quad \left(\beta_1 = \frac{\alpha(\theta^2+\alpha^2)}{\theta^2+\alpha^2(1+\gamma)}\right).$$



Matched Asymptotics: Outer region $(R_0, S^{\pm}, X_+ = X_- = X^*)$

- $O(1)$

$$0 = F(R, S)$$

- $O(\varepsilon)$

$$\frac{d^2R}{dX^2} = \frac{\theta}{2\delta}(R+S) - \alpha,$$
$$\frac{d^2S}{dX^2} = \frac{\theta}{2\delta}(R+S) + \alpha - 2\beta_1\psi + \chi(R,S)$$

Where:

$$\chi(R,S) \sim O(\varepsilon), \quad \psi(u^2) = \frac{\gamma u^2}{1+u^2} + 1$$

Matched Asymptotics: Outer region $(R_0, S^{\pm}, X_+ = X_- = X^*)$

• $O(1)$

$$0 = F(R, S) \to S(R, \hat{u}) = \varphi_1(\hat{u})R + \varphi_0(\hat{u}).$$

• $O(\varepsilon)$

$$\frac{d^2R}{dX^2} = \frac{\theta}{2\delta}(R + S) - \alpha,$$

$$\frac{d^2S}{dX^2} = \frac{\theta}{2\delta}(R + S) + \alpha - 2\beta_1\psi + \chi(R, S)$$

Where:

$$\chi(R, S) \sim O(\varepsilon), \quad \psi(u^2) = \frac{\gamma u^2}{1 + u^2} + 1$$

Choosing:

$$\hat{u} = \begin{cases} u_0 = \alpha/\theta & X \in [-\mathcal{L}, X^*], \\ u_+ = (R_0 + S_+)/(2\delta) & X \in [X*, 0] \end{cases}$$

Matched Asymptotics: Outer region $(R_0, S^{\pm}, X_+ = X_- = X^*)$

$$R(X) = \begin{cases} R_1(X) = \zeta(u_0) + (R_0 - \zeta(u_0)) \frac{\cosh(\sigma(u_0)(X+\mathcal{L}))}{\cosh(\sigma(u_0)(X^*+\mathcal{L}))} & X \in [-\mathcal{L}, X^*], \\ R_3(X) = \zeta(u_+) + (R_0 - \zeta(u_+)) \frac{\cosh(\sigma(u_+)x)}{\cosh(\sigma(u_+)X^*)} & X \in [X^*, 0] \end{cases}$$

and

$$S(X) = \begin{cases} \varphi_1(u_0)R_1(X) + \varphi_0(u_0) & X \in [-\mathcal{L}, X^*], \\ \varphi_1(u_+)R_3(X) + \varphi_0(u_+) & X \in [X^*, 0]. \end{cases}$$

Where

$$\zeta(u) = v(u) + \frac{\alpha\delta}{\theta} + v'(u)\left(\frac{\alpha}{\theta} - u\right), \qquad \sigma(u) = \sqrt{\frac{\theta}{\delta + v'(u)}}.$$

Matched Asymptotics: Matching condition.

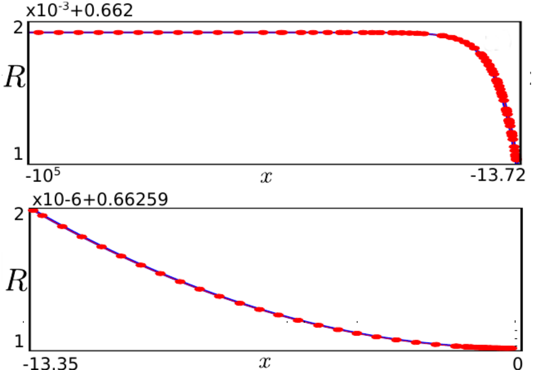
Imposing the following matching condition

$$\frac{d}{dX}(R,S)\Big|_{x=x_-} = \frac{d}{dX}(R,S)\Big|_{x=x_+},$$

and approximating $\tanh(\sigma(u_0)(X*+\mathcal{L}))\approx 1$, $\tanh(\sigma(u_+)X^*)\approx\sigma(u_+)X^*$, we obtain:

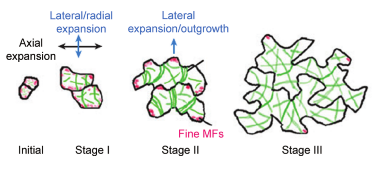
$$X^* = \frac{\sigma(u_0)(R_0-\zeta(u_0))}{\sigma(u_+)^2(R_0-\zeta(u_+))}. \quad (u_0=\alpha/\theta)$$

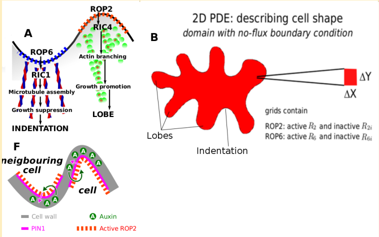
Given R_0, for $\varepsilon = 10^{-9}$:



Pavement cells (Preliminary).

Experimental observations





Reproduced from [Lin et al. 2014]. Cotyledon of

Reproduced from [Grieneisen et al. 2012]

Pavement cells (preliminary).

$$\partial_t \vec{c} = \underbrace{\partial_{\gamma\gamma}\vec{c}}_{\text{curve shortening}} + \underbrace{\vec{c}_\theta}_{\text{opposite curvature}} + \underbrace{(\vec{c}_\theta - \vec{c})}_{\text{stationary shape}} + \underbrace{\eta(\gamma)\hat{n}}_{\text{anisotropy}}$$

Conclusions and Future Research.

Conclusions.

1. **Adding source and loss terms to the wave pinning model** we found
   - 2 types of localised structures: spikes and snakes.
   - Transition between spikes and snakes, BD point.
   - Limit $\varepsilon \to 0$ connects spikes with fronts.
   - Match Asymptotics in the limit $\varepsilon \to 0$ in terms of R_0.
2. **Pavement cells (Preliminary)** A generalised version of the curve-shortening flow problem, is proposed to describe the dynamics in the membrane.

Conclusions and Future Research.

Future Research.

1. **Matching Asymptotics:** Find Analytically R_0 from an additional matching condition.
2. **Pavement cells:** Refine the model for pavement cells (e.g. consider more than one cell, couple the model with the *ROPs* model.).

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