Self-Organisation in Reaction-Diffusion Systems

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" . . . Later in the book we discuss in considerable detail various possible mechanisms for generating spatial patterns, including reaction-diffusion systems. I firmly believe that the process here is mechanistic and *not* genetic."

— J. D. Murray, *Mathematical Biology*

Overview

Mathematical models of morphogenesis

- chemical gradients influence fate of surrounding tissue
- cell differentiation
- tissue and organ formation – epidermal appendages (hairs, feathers)
- mathematical model for the chemical basis of morphogenesis – Turing (1952)
- activator-inhibitor model – Gierer and Meinhardt (1972)
- various models for generation of spatial patterns (spatial heterogeneity)

Turing's model

- reaction kinetic system

$$(u, v)_t = F(u, v), \quad u, v \in \mathbb{R}, \quad F : \mathbb{R}^2 \to \mathbb{R}^2$$

- steady state $(\hat{u}, \hat{v}) : F(\hat{u}, \hat{v}) = 0$
- asymptotically stable to spatially homogeneous perturbations
- reaction-**diffusion** system

$$(u, v)_t = D\nabla^2(u, v) + F(u, v)$$

- unstable to spatially heterogeneous perturbations
- $D \neq I$ – diffusion rates for u, v must be different

Gierer and Meinhardt's model

$$
\begin{aligned}
u_t - d_u \Delta u &= \frac{u^p}{v^q} + \sigma_1(x) - \mu_u u \quad \text{in } [0, T) \times \Omega \\
v_t - d_v \Delta v &= \frac{u^r}{v^s} + \sigma_2(x) - \mu_v v \quad \text{in } [0, T) \times \Omega
\end{aligned} \tag{1}
$$

- Ω is a bounded smooth domain in $\mathbb{R}^n$, and $T \in (0, \infty]$
- initial data $u(0, \cdot), v(0, \cdot) \in L^\infty(\Omega)$
- homogeneous Neumann boundary conditions

$$
\mathbf{n} \cdot \nabla u = \mathbf{n} \cdot \nabla v = 0 \quad \text{in } \partial\Omega
$$

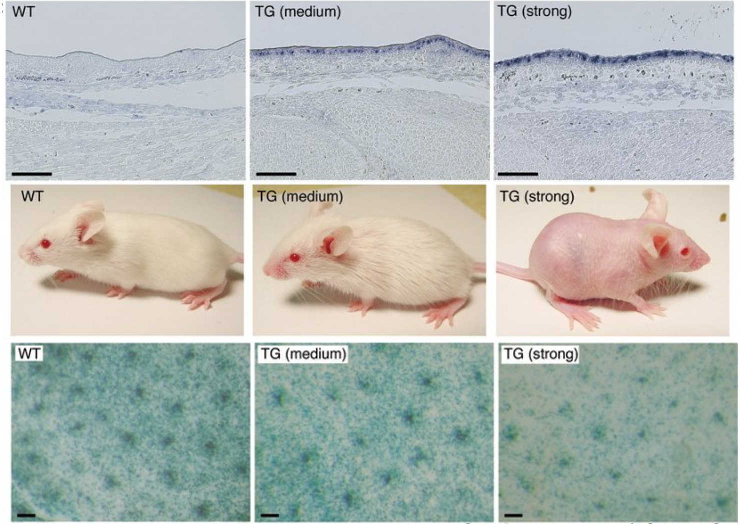
- $p = r = 2, q = 1, s = 0$, Turing space (μ_u, μ_v)
- vast literature on existence and uniqueness of solutions for different p, q, r, s, σ_i

Gierer and Meinhardt's model

(Loading movie...)

Model for hair follicle localisation in mice

wild-type mouse vs. DKK-transgenetic mutant mouse



Sick, Reinker, Timmer & Schlake, *Science*, 314, 2006.

Model for hair follicle spacing in mice

[Sick et al., 2006]

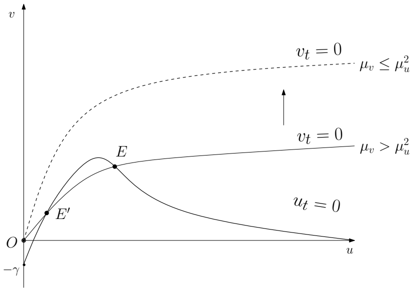
- WNT signalling pathway in hair follicle localisation
- DKK has inhibitory effect on WNT
- GM kinetics with saturation, Turing instability
- identical production term for activator u & inhibitor v

$$
\begin{aligned}
u_t - d_u \nabla^2 u &= \frac{\rho_u}{v+\gamma} \cdot \frac{u^2}{1+\kappa u^2} - \mu_u u \quad \text{in } [0,T) \times \Omega \\
v_t - d_v \nabla^2 v &= \frac{\rho_v}{v+\gamma} \cdot \frac{u^2}{1+\kappa u^2} - \mu_v v \quad \text{in } [0,T) \times \Omega
\end{aligned} \tag{2}
$$

Reaction-kinetic system

- GM type without source terms
- normalise $\rho_u = \rho_v = 1, \quad \mu_u := \frac{\mu_u}{\rho_u}, \quad \mu_v := \frac{\mu_v}{\rho_v}$

$$
\begin{aligned}
u_t &= \frac{u^2}{(v+\gamma)(1+\kappa u^2)} - \mu_u u \\
v_t &= \frac{u^2}{(v+\gamma)(1+\kappa u^2)} - \mu_v v
\end{aligned}
$$



Analytical properties

- solution (u, v) of (2) has global existence in L^∞ on $(0, \infty] \times \Omega$ for strictly positive initial data in L^∞
- $(0, 0)$ is the unique homogeneous steady state for $\mu_v < \mu_u^2$ (corresponds to values used by Sick et al. (2006))

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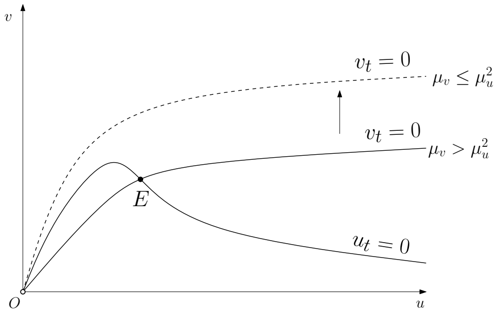
Limiting form of model system

$$
\begin{aligned}
u_t - d_u \nabla^2 u &= \frac{u^2}{v(1+\kappa u^2)} - \mu_u u \quad \text{in } [0,T) \times \Omega \\
v_t - d_v \nabla^2 v &= \frac{u^2}{v(1+\kappa u^2)} - \mu_v v \quad \text{in } [0,T) \times \Omega
\end{aligned}
\tag{3}
$$

- $\gamma = 0, d_u = 1, d_v = d$ – approximation when $\gamma \approx 0$
- solution (u, v) of (3) has global existence in L^∞ on $(0, \infty] \times \Omega$ for strictly positive initial data in L^∞
- a-priori bounds on stationary solutions in t
- find Turing space

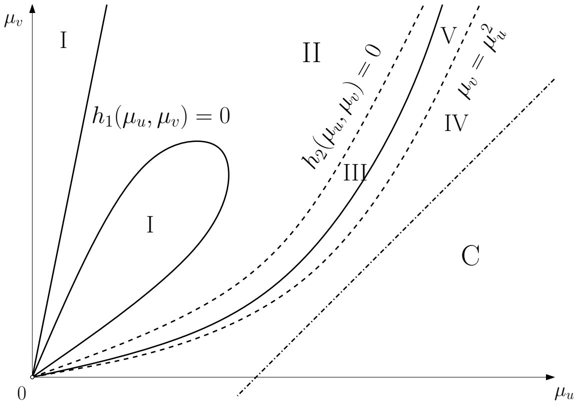
Modified model, phase portrait



- $\mu_u^2 \geq \mu_v$: no homogeneous steady state for (3)
- O is a singularity for the reaction kinetic system
- when $\mu_u > \mu_v$, for appropriately chosen initial data u_0, v_0 the solutions of (3)

$$u, v \to 0 \text{ uniformly on } \Omega, \quad t \to \infty$$

Turing space for fixed Ω, d, κ



subregion V – Turing instability, subregion C – collapsing solutions
subregion IV – far-from-equilibrium stationary solutions

Summary

- "modified" GM – uniform boundedness, global existence
- conditions for pattern formation in Sick et al. (2006) not relevant
- patterns observed are not due to Turing bifurcation, but convergence to a far-from-equilibrium solution
- sensitivity to initial conditions because of collapsing solutions

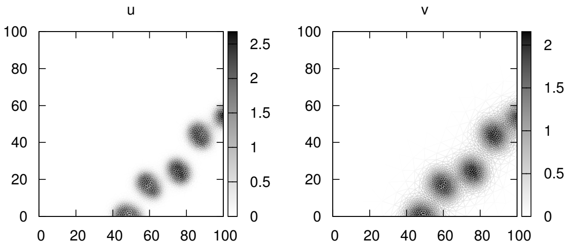


Figure: Asymmetric pattern converging to some non-trivial solution branch stemming from some (unknown) steady state

Literature

- P. Rashkov.
  Remarks on pattern formation in a model for hair follicle spacing.
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  Regular and discontinuous solutions in a reaction-diffusion model for hair follicle spacing.
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- S. Sick, S. Reinker, J. Timmer, and T. Schlake.
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LOEWE

Exzellente Forschung für Hessens Zukunft

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