Distributed Delays in Reaction-Diffusion Systems

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What is a Turing pattern ? [8]

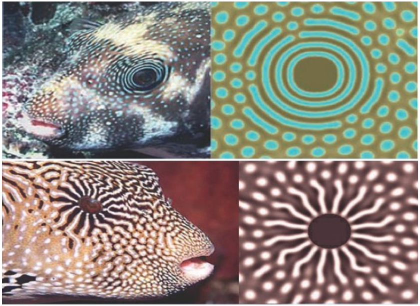
- Turing proposed chemical basis for biological pattern formation (Reaction-Diffusion systems) [9].
- Turing (diffusion-driven) instability: spatially homogeneous steady state $+$*diffusion* $\implies$ spatially inhomogenous steady-state.

$$u_t = \nabla^2 u + f(u, v), \qquad v_t = d\nabla^2 v + g(u, v) \tag{1}$$

- Linearising about steady-state (no diffusion):
  - $f_u + g_v < 0, \qquad f_u g_v - f_v g_u > 0$
- Linearising about steady-state (with diffusion):
  - $df_u + g_v > 0, \qquad (df_u + g_v)^2 - 4d(f_u g_v - f_v g_u) > 0$

Turing patterns in nature

(a) Image taken from [1]



(b) Image taken from [2]

Figure 1: Patterns found in nature

Mathematical Model (Without delay)

- Schnakenberg Kinetics. $u = u(x,t), v = v(x,t)$.

$$\begin{pmatrix} u_t \\ v_t \end{pmatrix} = \begin{pmatrix} u_{xx} \\ dv_{xx} \end{pmatrix} + \begin{pmatrix} a - u + u^2 v \\ b - u^2 v \end{pmatrix} \tag{2}$$

- Conditions for Turing instability:
  - $0 < b - a < (a+b)^3$
  - $(a+b)^2 > 0$
  - $d(b-a) > (a+b)^3$
  - $\left[d(b-a) - (a+b)^3\right]^2 > 4d(a+b)^4$

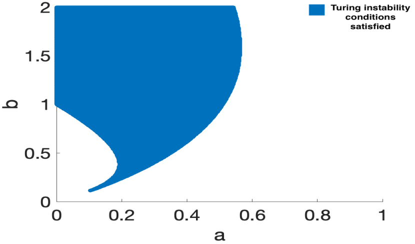
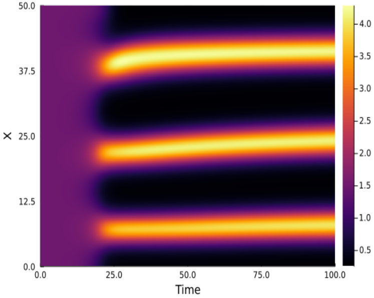


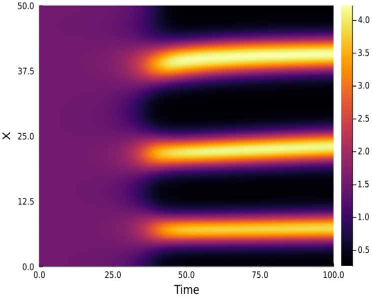
Figure 2: Turing space produced in MATLAB

Research Aims

- Question: How does (distributed) delay affect the propensity for Turing instability and pattern formation ?
- Motivation:
  - Time-delays affect behaviour of dynamical systems.
  - Arise naturally in gene-expression process.
  - Can affect the type and timing of pattern formation that we see.



(a) Example of Turing pattern produced in Julia (without delay)



(b) Example of Turing pattern produced in Julia (with delay)

Biological Motivation [5, 3]

- Ability of cell to adopt state relevant to its spatial and temporal position (Differential gene expression).
- Cell-signalling: co-ordination among cells.
- Cell-signalling influence the gene-expression process, ultimately resulting in spatial pattern formation.
- Gene expression is complex (gene-transcription, translation) with time-delays (in reality are stochastic.)

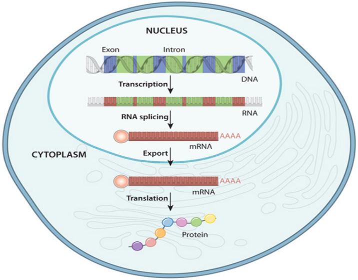


Figure 4: An overview of the flow of information from DNA to protein in a cell [2]

Mathematical Model (With delay)

- Ligand-Internalisation model. $u = u(x,t), v = v(x,t)$.
  - With fixed time-delay

$$\begin{pmatrix} u_t \\ v_t \end{pmatrix} = \begin{pmatrix} u_{xx} \\ dv_{xx} \end{pmatrix} + \begin{pmatrix} a - u - 2u^2 v + 3u^2(t-\tau)v(t-\tau) \\ b - u^2 v \end{pmatrix} \tag{3}$$

  - With distributed time-delay

$$\begin{pmatrix} u_t \\ v_t \end{pmatrix} = \begin{pmatrix} u_{xx} \\ dv_{xx} \end{pmatrix} + \begin{pmatrix} a - u - 2u^2 v + 3\int_0^{2\tau} k(s,\tau,\sigma)u^2(t-s)v(t-s)ds \\ b - u^2 v \end{pmatrix} \tag{4}$$

$k(s,\tau,\sigma)$ truncated Gaussion pdf, mean: τ, standard deviation: σ.

We consider homogeneous Neumann boundary conditions (self-organisation), and restrict our investigation to one spatial dimension.

Current Literature

- Currently literature mostly describes the fixed delay case [5, 4, 10]. Fixed delays can:
  - Increase time to pattern formation.
  - Result in temporal oscillations (shrinking Turing space.)
  - Increase sensitivity of patterns to initial conditions.

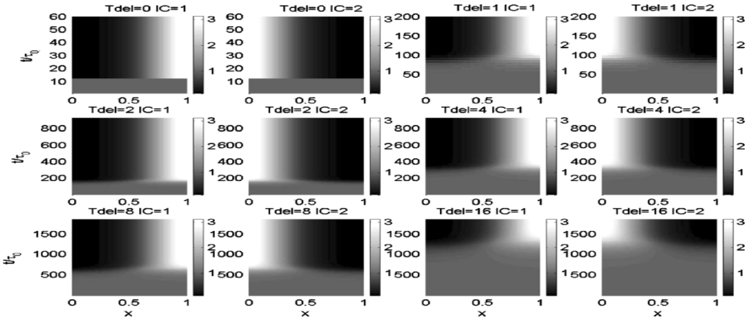


Figure 5: Result of fixed time-delay [5]

- Does distributed delay alleviate (or worsen) some of these problems ?

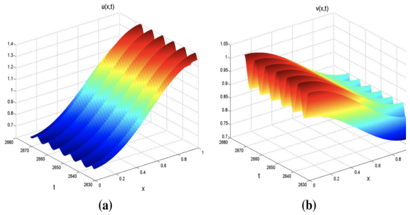
Report Structure (1)

- 1. Development and validation of tools
  - Gauss-Hermite quadrature to approximate distributed delay as a set of N fixed delay. Integrals of the form

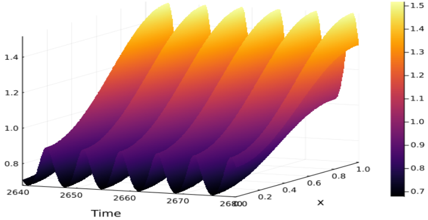
$$\int_{-\infty}^{\infty} e^{-x^2} f(x) \approx \sum_{i=1}^{N} w_i f(x_i) \tag{5}$$

    - ⋆ Quadrature method builds off work in [3].
  - Use Julia to numerically solve stiff DDEs.
    - ⋆ Efficient code for our purposes.
  - Verify results against current literature/analytical examples/convergence analysis.

- 2. Review of current literature and further analysis (Fixed delay)
  - Validation of results.
  - Sensitivity of results to initial conditions - systematic extension.
  - How do varying model parameters affect these results.
    - ★ Higher risk: depends on computational limits

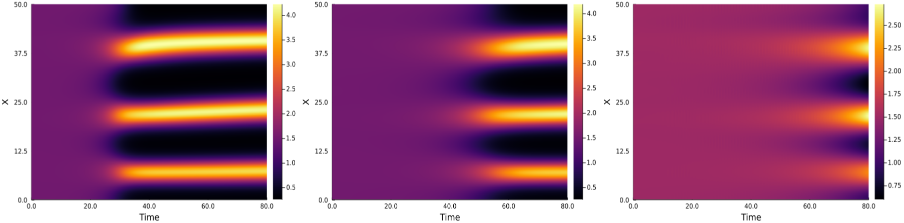


(a) Results produced in [6]



(b) Results reproduced in Julia

- 3. Incorporate distribution
  - Analysis of varying σ
    - ★ No current literature on distributed delay in Schnakenberg model.
    - ★ Previous dissertation - preliminary results.
  - Consider different distributions/delay terms
    - ★ Higher risk: depends on research time limits



(a) $\tau = 0.4, \sigma = 0.1$ (b) $\tau = 0.6, \sigma = 0.01$ (c) $\tau = 0.8, \sigma = 0.01$

Figure 7: Results produced in Julia

Report Structure (4)

- 4. Summary and Conclusion
    - Developed efficient code to numerically solve stiff DDEs.
    - Evaluation of current literature for fixed delays and systematic extension.
    - Understanding impact of distributed delays.
    - Goal: Does the prospect of Turing patterns increase or decrease with distributed delays.

References

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[5] EA Gaffney and NAM Monk. "Gene expression time delays and Turing pattern formation systems". In: *Bulletin of mathematical biology* 68.1 (2006), pp. 99–130.

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[7] Hans Meinhardt. *The algorithmic beauty of sea shells*. Springer Science & Business Media, 2009.

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