Monotone Dynamical Systems: A Quick Tour

Hal Smith



H.L. Smith (ASU)

Monotone Dynamical Systems

Sontagfest, May 23, 2011 1 / 16

Monotone Dynamical System

- State space: metric space (X, d) with a closed* partial order relation ≤. (x_n ≤ y_n ∧ x_n → x ∧ y_n → y ⇒ x ≤ y)
 Dynamics: discrete-time (T = Z₊) or continuous-time
 - $(T = \mathbb{R}_+)$ semiflow $\Phi: T \times X \to X$. Notation $\Phi_t(x) = \Phi(t, x)$:
 - Φ continuous.
 - $\Phi_0 = id_X$
 - $\Phi_t \circ \Phi_s = \Phi_{t+s}, \quad t, s \in T$
- **Order-Preserving:** $x \le y \Rightarrow \Phi_t(x) \le \Phi_t(y), t \in T, x, y \in X.$

Trivial Examples:

•
$$X = \mathbb{R}$$
, usual order \leq , $x' = f(x)$, $\Phi_t(x_0) = x(t, x_0)$.

- $X = BC(\mathbb{R}, \mathbb{R})$, usual order \leq , $u_t = u_{xx} + f(x, u)$, $\Phi_t(u_0) = u(t, \cdot)$.
- $X = \mathbb{R}, f \nearrow, x(n+1) = f(x(n)), n \ge 0, \Phi_n(x(0)) = f^{(n)}(x(0)).$

standing assumptions:

 $\bigcirc T = \mathbb{R}_+.$

 $\forall x \in X, \{\Phi_t(x) : t \ge 0\}$ has compact closure in X.

H.L. Smith (ASU)

Monotone Dynamical System

- State space: metric space (X, d) with a closed* partial order relation ≤. (x_n ≤ y_n ∧ x_n → x ∧ y_n → y ⇒ x ≤ y)
 Dynamics: discrete-time (T = Z₊) or continuous-time
 - $(T = \mathbb{R}_+)$ semiflow $\Phi: T \times X \to X$. Notation $\Phi_t(x) = \Phi(t, x)$:
 - Φ continuous.
 - $\Phi_0 = id_X$
 - $\Phi_t \circ \Phi_s = \Phi_{t+s}, \quad t, s \in T$
- **Order-Preserving:** $x \le y \Rightarrow \Phi_t(x) \le \Phi_t(y), t \in T, x, y \in X.$

Trivial Examples:

- $X = \mathbb{R}$, usual order \leq , x' = f(x), $\Phi_t(x_0) = x(t, x_0)$.
- $X = BC(\mathbb{R}, \mathbb{R})$, usual order \leq , $u_t = u_{xx} + f(x, u)$, $\Phi_t(u_0) = u(t, \cdot)$.
- $X = \mathbb{R}, f \nearrow, x(n+1) = f(x(n)), n \ge 0, \Phi_n(x(0)) = f^{(n)}(x(0)).$

standing assumptions:

 $\bigcirc T = \mathbb{R}_+.$

 $\forall x \in X, \{\Phi_t(x) : t \ge 0\}$ has compact closure in X.

H.L. Smith (ASU)

Monotone Dynamical Systems

イロト 不得 トイヨト イヨト ニヨー

Monotone Dynamical System

- State space: metric space (X, d) with a closed* partial order relation ≤. ^{*}(x_n ≤ y_n ∧ x_n → x ∧ y_n → y ⇒ x ≤ y)
 Dynamics: discrete time (T → Z) or continuous time.
- **2** Dynamics: discrete-time $(T = \mathbb{Z}_+)$ or continuous-time $(T = \mathbb{R}_+)$ semiflow $\Phi : T \times X \to X$. Notation $\Phi_t(x) = \Phi(t, x)$:
 - Φ continuous.
 - $\Phi_0 = id_X$
 - $\Phi_t \circ \Phi_s = \Phi_{t+s}, \quad t, s \in T$
- **Order-Preserving:** $x \le y \Rightarrow \Phi_t(x) \le \Phi_t(y), t \in T, x, y \in X.$

Trivial Examples:

- $X = \mathbb{R}$, usual order \leq , x' = f(x), $\Phi_t(x_0) = x(t, x_0)$.
- $X = BC(\mathbb{R}, \mathbb{R})$, usual order \leq , $u_t = u_{xx} + f(x, u)$, $\Phi_t(u_0) = u(t, \cdot)$.
- $X = \mathbb{R}, f \nearrow, x(n+1) = f(x(n)), n \ge 0, \Phi_n(x(0)) = f^{(n)}(x(0)).$

standing assumptions:

- $T = \mathbb{R}_+$.
- $\forall x \in X, \{\Phi_t(x) : t \ge 0\}$ has compact closure in X.

H.L. Smith (ASU)

Monotone Dynamical Systems

 $X \subset Y$, Y an ordered Banach space with closed positive cone Y_+ :

$$\mathbb{R}_{+})Y_{+} \subset Y_{+}, \ Y_{+} + Y_{+} \subset Y_{+}, \ (Y_{+}) \cap (-Y_{+}) = \{0\}$$

Partial order: $y \le x \Leftrightarrow x - y \in Y_+$

Y is strongly ordered if Int $Y_+ \neq \emptyset$. Then $y \ll x \Leftrightarrow x - y \in Int Y_+$.

Examples:

•
$$Y = \mathbb{R}^n, Y_+ = \mathbb{R}^k_+ \times (-\mathbb{R}^{n-k}_+), 0 \le k \le n$$
:

 $x \leq y \Leftrightarrow (x_i \leq y_i, \ i \leq k) \land (x_j \geq y_j, \ j > k)$

• $Y = L^{p}(\Omega, \mathbb{R}^{n}), \ C^{r}(\Omega, \mathbb{R}^{n}), \ f \leq g \Leftrightarrow f(s) \leq g(s), \ s \in \Omega$

< ロ > < 同 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ >

 $X \subset Y$, Y an ordered Banach space with closed positive cone Y_+ :

$$(\mathbb{R}_+)Y_+ \subset Y_+, \ Y_+ + Y_+ \subset Y_+, \ (Y_+) \cap (-Y_+) = \{0\}$$

Partial order: $y \le x \Leftrightarrow x - y \in Y_+$

Y is strongly ordered if Int $Y_+ \neq \emptyset$. Then $y \ll x \Leftrightarrow x - y \in Int Y_+$.

Examples:

•
$$Y = \mathbb{R}^n$$
, $Y_+ = \mathbb{R}^k_+ \times (-\mathbb{R}^{n-k}_+)$, $0 \le k \le n$:

 $x \leq y \Leftrightarrow (x_i \leq y_i, \ i \leq k) \land (x_j \geq y_j, \ j > k)$

• $Y = L^{p}(\Omega, \mathbb{R}^{n}), \ C^{r}(\Omega, \mathbb{R}^{n}), \ f \leq g \Leftrightarrow f(s) \leq g(s), \ s \in \Omega$

 $X \subset Y$, Y an ordered Banach space with closed positive cone Y_+ :

$$(\mathbb{R}_+)Y_+ \subset Y_+, \ Y_+ + Y_+ \subset Y_+, \ (Y_+) \cap (-Y_+) = \{0\}$$

Partial order: $y \le x \Leftrightarrow x - y \in Y_+$

Y is strongly ordered if Int $Y_+ \neq \emptyset$. Then $y \ll x \Leftrightarrow x - y \in Int Y_+$.

Examples:

•
$$Y = \mathbb{R}^n, Y_+ = \mathbb{R}^k_+ \times (-\mathbb{R}^{n-k}_+), 0 \le k \le n$$
:
 $x \le y \Leftrightarrow (x_i \le y_i, i \le k) \land (x_j \ge y_j, j > k)$

• $Y = L^{p}(\Omega, \mathbb{R}^{n}), \ C^{r}(\Omega, \mathbb{R}^{n}), \ f \leq g \Leftrightarrow f(s) \leq g(s), \ s \in \Omega$

Equilibria:
$$E = \{e \in X : \forall t \ge 0, \Phi_t(e) = e\}$$

Sub-equilibria: $E_{-} = \{x \in X : \forall t \ge 0, \Phi_t(x) \ge x\}$

$$x \in E_{-} \Rightarrow x \leq \Phi_{s}(x) \leq \Phi_{t+s}(x), t, s \geq 0$$

 $\therefore \Phi_t(\mathbf{x}) \nearrow \mathbf{e} \in E, \ t \nearrow \infty.$

Super-equilibria: { $x \in X : \forall t \ge 0, \Phi_t(x) \le x$ }

in applications, these can be identified by the semiflow generator

Equilibria:
$$E = \{e \in X : \forall t \ge 0, \Phi_t(e) = e\}$$

Sub-equilibria: $E_{-} = \{x \in X : \forall t \ge 0, \Phi_t(x) \ge x\}$

 $\mathbf{x} \in \mathbf{E}_{-} \Rightarrow \mathbf{x} \leq \Phi_{\mathbf{s}}(\mathbf{x}) \leq \Phi_{t+\mathbf{s}}(\mathbf{x}), \ t, \mathbf{s} \geq 0$

 $\therefore \Phi_t(\mathbf{x}) \nearrow \mathbf{e} \in E, \ t \nearrow \infty.$

Super-equilibria: { $x \in X : \forall t \ge 0, \Phi_t(x) \le x$ }

in applications, these can be identified by the semiflow generator

Equilibria: $E = \{e \in X : \forall t \ge 0, \Phi_t(e) = e\}$

Sub-equilibria: $E_{-} = \{x \in X : \forall t \ge 0, \Phi_t(x) \ge x\}$

 $x \in E_{-} \Rightarrow x \leq \Phi_{s}(x) \leq \Phi_{t+s}(x), \ t, s \geq 0$ $\therefore \Phi_{t}(x) \nearrow e \in E, \ t \nearrow \infty.$

Super-equilibria: { $x \in X : \forall t \ge 0, \Phi_t(x) \le x$ }

in applications, these can be identified by the semiflow generator

Equilibria:
$$E = \{e \in X : \forall t \ge 0, \Phi_t(e) = e\}$$

Sub-equilibria: $E_{-} = \{x \in X : \forall t \ge 0, \Phi_t(x) \ge x\}$

$$x \in E_{-} \Rightarrow x \leq \Phi_{s}(x) \leq \Phi_{t+s}(x), t, s \geq 0$$

 $\therefore \Phi_{t}(x) \nearrow e \in E, t \nearrow \infty.$

Super-equilibria: { $x \in X : \forall t \ge 0, \Phi_t(x) \le x$ }

in applications, these can be identified by the semiflow generator

Sub & Super Equilibria Bracket Basin

 x_1 is a sub-equilibrium with $\Phi_t(x_1) \nearrow e \in E$. Monotonicity implies

 $B = \{x \in X : x_1 \le x \le e\} \subset$ Basin of attraction of e

because it is "sandwiched": $\Phi_t(x_1) \le \Phi_t(x) \le \Phi_t(e) = e$



H.L. Smith (ASU)

Strong Monotonicity & Limit Set Dichotomy

 Φ strongly monotone (Hirsch) if Y is strongly ordered and $x < y \Rightarrow \Phi_t(x) \ll \Phi_t(y), t > 0.$

Φ is strongly order preserving (Matano) (SOP) if it is monotone and $x < y \Rightarrow \exists$ nbhds $U, V, x ∈ U, y ∈ V, \exists t_0 ≥ 0$ such that

 $\Phi_{t_0}(U) \leq \Phi_{t_0}(V)$

Theorem[LSD, Hirsch(1982)]: Let Φ be SOP. If x < y then either (a) $\omega(x) < \omega(y)$, or (b) $\omega(x) = \omega(y) \subset E$

 $\omega(x) =$ omega limit set of x

Strong Monotonicity & Limit Set Dichotomy

 Φ strongly monotone (Hirsch) if Y is strongly ordered and $x < y \Rightarrow \Phi_t(x) \ll \Phi_t(y), t > 0.$

Φ is strongly order preserving (Matano) (SOP) if it is monotone and $x < y \Rightarrow \exists$ nbhds $U, V, x ∈ U, y ∈ V, \exists t_0 ≥ 0$ such that

 $\Phi_{t_0}(U) \leq \Phi_{t_0}(V)$

Theorem[LSD, Hirsch(1982)]: Let Φ be SOP. If x < y then either (a) $\omega(x) < \omega(y)$, or (b) $\omega(x) = \omega(y) \subset E$

 $\omega(x) = \text{omega limit set of } x$

Theorem*: Assume $X \subset Y$, Y an ordered Banach space, and X is either convex or the closure of an open set. Let

$$C = \{x \in X : \Phi_t(x) \rightarrow e, e \in \text{Equilibria}\}$$

If Φ is SOP on X and some mild smoothness and compactness assumptions hold (†), then Int C is dense in X.

*Inspired by: M. Hirsch. Systems of differential equations which are competitive or cooperative II: convergence almost everywhere, SIAM J. Math. Anal., 16, 1985.

 $(\dagger) \exists \tau > 0$:

$$x_1 < x_2 \Rightarrow \Phi_{\tau} x_1 \ll \Phi_{\tau} x_2$$

• Φ_{τ} is locally C^1 at each $e \in E$, $\Phi'_{\tau}(e)$ is Krein-Rutman operator.

< ロ > < 同 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < 回 > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ > < □ >

ODEs-A Canonical Form

x' = F(x) is a monotone system w.r.t. **orthant cone** $\mathbb{R}^k_+ \times (-\mathbb{R}^{n-k}_+)$ in domain X if, on permuting variables $x = (x_1, x_2), x_1 \in \mathbb{R}^k, x_2 \in \mathbb{R}^{n-k}$

$$\begin{array}{rcl} x_1' &=& f_1(x_1,x_2) \\ x_2' &=& f_2(x_1,x_2) \end{array}$$

• diagonal blocks $\frac{\partial f_i}{\partial x_i}(x)$ have nonnegative off-diagonal entries.

• off-diagonal blocks $\frac{\partial f_i}{\partial x_i}(x) \leq 0$, $i \neq j$ have nonpositive entries.

Jacobian =
$$\begin{bmatrix} * & + & - & - \\ + & * & - & - \\ - & - & * & + \\ - & - & + & * \end{bmatrix}, \ + \ge 0, \ - \le 0$$

Components cluster into two subgroups. positive within-group interactions, negative between-group interactions.

Strong monotonicity holds if the Jacobian is irreducible at a.e. * C. *!. = on

H.L. Smith (ASU)

Monotone Dynamical Systems

ODEs-A Canonical Form

x' = F(x) is a monotone system w.r.t. **orthant cone** $\mathbb{R}^k_+ \times (-\mathbb{R}^{n-k}_+)$ in domain X if, on permuting variables $x = (x_1, x_2), x_1 \in \mathbb{R}^k, x_2 \in \mathbb{R}^{n-k}$

$$\begin{array}{rcl} x_1' &=& f_1(x_1,x_2) \\ x_2' &=& f_2(x_1,x_2) \end{array}$$

• diagonal blocks $\frac{\partial f_i}{\partial x_i}(x)$ have nonnegative off-diagonal entries.

• off-diagonal blocks $\frac{\partial f_i}{\partial x_i}(x) \leq 0$, $i \neq j$ have nonpositive entries.

Jacobian =
$$\begin{bmatrix} * & + & - & - \\ + & * & - & - \\ - & - & * & + \\ - & - & + & * \end{bmatrix}, \ + \ge 0, \ - \le 0$$

Components cluster into two subgroups. positive within-group interactions, negative between-group interactions.

Strong monotonicity holds if the Jacobian is irreducible at a.e. * CAL = 30

H.L. Smith (ASU)

Monotone Dynamical Systems

ODEs-A Canonical Form

x' = F(x) is a monotone system w.r.t. **orthant cone** $\mathbb{R}^k_+ \times (-\mathbb{R}^{n-k}_+)$ in domain X if, on permuting variables $x = (x_1, x_2), x_1 \in \mathbb{R}^k, x_2 \in \mathbb{R}^{n-k}$

$$\begin{array}{rcl} x_1' &=& f_1(x_1,x_2) \\ x_2' &=& f_2(x_1,x_2) \end{array}$$

• diagonal blocks $\frac{\partial f_i}{\partial x_i}(x)$ have nonnegative off-diagonal entries.

• off-diagonal blocks $\frac{\partial f_i}{\partial x_i}(x) \leq 0$, $i \neq j$ have nonpositive entries.

Jacobian =
$$\begin{bmatrix} * & + & - & - \\ + & * & - & - \\ - & - & * & + \\ - & - & + & * \end{bmatrix}, \ + \ge 0, \ - \le 0$$

Components cluster into two subgroups. positive within-group interactions, negative between-group interactions.

Strong monotonicity holds if the Jacobian is irreducible at a.e. $x \in X!$

H.L. Smith (ASU)

Monotone Dynamical Systems

Repressilator with 2 genes

- $x_i =$ [protein] product of gene i $y_i =$ [mRNA] of gene i.
- x_{i-1} represses transcription of y_i :

$$egin{array}{rcl} x'_i &=& eta_i(y_i - x_i) \ y'_i &=& lpha_i f_i(x_{i-1}) - y_i, \ i = 1, 2, \ \ \mbox{mod} \ 2 \end{array}$$

where $\alpha_i, \beta_i > 0$ and $f_i > 0$ satisfies $f'_i < 0$.

$$Jacobian = \begin{bmatrix} - + & 0 & 0 \\ 0 & - & - & 0 \\ 0 & 0 & - & + \\ - & 0 & 0 & - \end{bmatrix}$$

Gardner et al, "Construction of a genetic toggle switch in E. coli", Nature(403),2000.

Dynamics of Repressilator

Equilibria $u = (x_1, y_1, x_2, y_2)$ are in 1-to-1 correspondence with fixed points of increasing map $g \equiv \alpha_2 f_2 \circ \alpha_1 f_1$



Theorem: If *g* has no degenerate fixed points, \exists odd number of equilibria $u^1, u^2, \dots, u^{2m+1}$ indexed by increasing values of x_2 . u_{2i+1} are stable, u_{2i} are unstable. If $B(u_i)$ denotes the basin of attraction of u_i , then

$$\cup_{\text{odd }i} B(u_i)$$

is open and dense in \mathbb{R}^4_+ . u_1 is globally attracting if m = 0.

H.L. Smith (ASU)

10/16

Repressilator with transcription and translation delays

$$\begin{aligned} x_i'(t) &= \beta_i [y_i(t - \mu_i) - x_i(t)] \\ y_i'(t) &= \alpha_i f_i(x_{i-1}(t - \tau_{i-1})) - y_i(t), \ i = 1,2 \end{aligned}$$

Generates a SOP semiflow on:

$$\begin{array}{lll} \mathcal{X} & = & \mathcal{C}([-\tau_1, 0], \mathbb{R}_+) \times \mathcal{C}([-\mu_1, 0], \mathbb{R}_+) \\ & & \times \mathcal{C}([-\tau_2, 0], \mathbb{R}_+) \times \mathcal{C}([-\mu_2, 0], \mathbb{R}_+) \end{array}$$

Previous Theorem holds without change for delayed repressilator. Extends to arbitrary even number of genes.

Test for Orthant-Cone Monotone ODE x' = f(x)

- $\forall i \neq j, \ \frac{\partial f_i}{\partial x_i}(x)$ does not change sign in X.
- Feedback Symmetry: $\frac{\partial f_i}{\partial x_i}(x) \frac{\partial f_j}{\partial x_i}(y) \ge 0, \ i \neq j$. golden rule
- Construct signed, influence graph:
 - un-directed edge joins *i* to $j \neq i$ if $\exists x \in X, \ \frac{\partial f_i}{\partial x_i}(x) \neq 0$.
 - append + sign to edge if derivative is positive, sign if negative.
- balanced graph (‡): every loop (cycle) has even number of "-" signs.

‡ This is Harary's Theorem: "a balanced network is clusterable". See "Networks: An Intro.", M. Newman An algorithm is given for clustering, i.e, permuting indices into subsets $I = \{1, 2, \dots, k\}$ and I^c .

Systems of Parabolic PDEs

Given elliptic operators L_i , the parabolic system

$$\begin{array}{rcl} \partial_t u_1 &=& L_1 u_1 + f_1(x, u_1, u_2) \\ \partial_t u_2 &=& L_2 u_2 + f_2(x, u_1, u_2), \ x \in \Omega, \ t > 0 \end{array}$$

where $f = (f_1(x, \cdot, \cdot), f_2(x, \cdot, \cdot))$ in canonical form, and boundary conditions

$$\mathbf{0} = \alpha_i \frac{\partial u_i}{\partial n} + \beta_i u_i, \ \mathbf{x} \in \partial \Omega$$

where $\alpha_i, \beta_i \ge 0$, generates a monotone semiflow on spaces

$$C^r_0(\overline{\Omega}) := \{ oldsymbol{v} \in oldsymbol{C}^r(\overline{\Omega}) : oldsymbol{v} | \partial \Omega = oldsymbol{0} \}$$

r = 0, 1 for Dirichlet B.C., or

$$C_{\alpha,\beta}^{r}(\overline{\Omega}) := \left\{ \boldsymbol{v} \in \boldsymbol{C}^{r}(\overline{\Omega}) : \beta \boldsymbol{v} + \alpha \frac{\partial \boldsymbol{v}}{\partial \boldsymbol{n}} = \boldsymbol{0}, \ \boldsymbol{x} \in \partial \Omega \right\}$$

for Robin or Neumann B.C.

H.L. Smith (ASU)

Convergence to uniform equilibria

$$u_t = D\nabla^2 u + f(u)$$

$$\frac{\partial u}{\partial n} = 0, x \in \partial \Omega$$

$$u(x,0) = u_0(x), x \in \Omega$$

 $\Omega \subset \mathbb{R}^n$ smooth, bounded, convex. $D = \text{diag}(d_i), d_i > 0.$ $f : \mathbb{R}^m \to \mathbb{R}^m$ is C^2 , cooperative, and irreducible.

Theorem[Enciso, Hirsch, S. (2008)]: Let solutions of u' = f(u) be bounded on $t \ge 0$. The set of $u_0 \in C(\overline{\Omega}, \mathbb{R}^m)$ such that u(x, t)converges to a spatially-uniform equilibrium is prevalent in $C(\overline{\Omega}, \mathbb{R}^m)$.

W is prevalent if its complement is shy. Borel set $W \subset X = C(\overline{\Omega}, \mathbb{R}^m)$ is shy if \exists a nonzero compactly supported Borel measure μ on *X*, such that $\mu(W + \mathbf{x}) = 0$, $\forall \mathbf{x} \in X$. Hunt, Sauer, Yorke, 1993

- Monotone Maps: No LSD, generic convergence to periodic points.
- Non-autonomous theory-Skew-Product Semiflows: J. Mierczynski, W. Shen, X. Zhao
- Monotone Random Systems: See I. Chueshov, Springer Lect. Notes in Math.
- Control Theory: Sontag, Angeli, De Leenheer, Enciso, Wang

My Favorite References

- Monotone Dynamical Systems, H.S. & M. Hirsch, Handbook of Differential Equations, Ordinary Differential Equations (volume 2), eds. A.Canada, P.Drabek, A.Fonda, Elsevier, 239-357, 2005.
- Monotone systems, a mini-review, H.S. & M.W. Hirsch, in Positive Systems. Proceedings of the First Multidisciplinary Symposium on Positive Systems (POSTA 2003). Luca Benvenuti, Alberto De Santis and Lorenzo Farina (Eds.) Lecture Notes on Control and Information Sciences vol. 294, Springer Verlag, Heidelberg, 2003.
- Monotone Maps: A Review, H.S.& M. Hirsch, J. Difference Eqns.& Appl. 11(2005) 379-398
- Monotone Dynamical Systems: an introduction to the theory of competitive and cooperative systems, Amer. Math. Soc. Surveys and Monograghs, 41, 1995.
- Systems of ordinary differential equations which generate an order preserving flow. A survey of results, SIAM Review 30, 1988.

▲□ ▶ ▲ □ ▶ ▲ □ ▶ □ ■ ● ● ● ●