Monotone Dynamical Systems: an Introduction

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Why Study Monotone Systems?

- **An easy to check sufficient condition for monotonicity**
- **Monotonicity implies strong global results**
- **Many applications in various fields of science**

Disclaimer

Generality and technical details are readily sacrificed for simplicity of presentation.

Monotone Systems-An Example

Consider the scalar linear system: $\dot{x}(t) = 17x(t)$.

The solution for $x(0) = a$ **is:**

$$x(t,a) = e^{17t}a.$$

Fix two initial conditions

$$a \leq b.$$

Then

$$x(t,a) = e^{17t}a \;\leq\; x(t,b) = e^{17t}b\,.$$

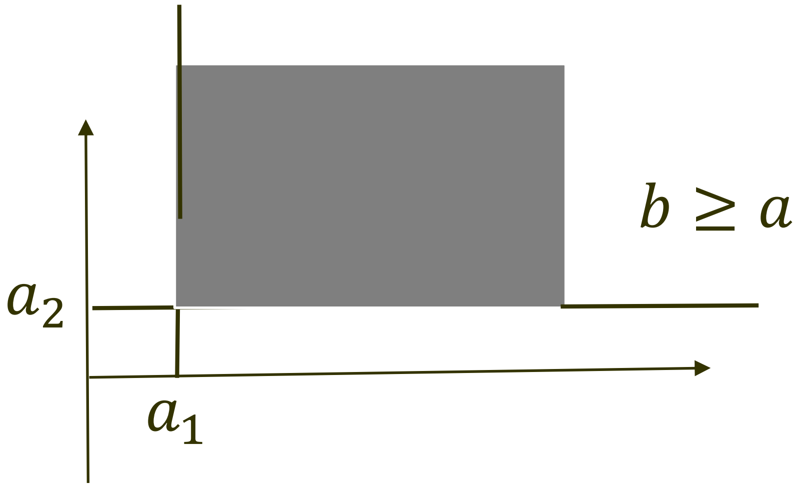
The solutions preserve the ordering between the initial conditions for all time t.

Monotone Systems-Definition

Notation For two vectors $a, b \in R^n$, $a \leq b$ **means that**

$$a_i \leq b_i, \qquad i = 1,2, \dots, n.$$

Example 1:



Example 2:

$$\begin{pmatrix} 2 \\ 4.32 \\ 3 \end{pmatrix} \leq \begin{pmatrix} 2.1 \\ 5 \\ 3 \end{pmatrix}.$$

Monotone Systems-Definition

Definition: **The system** $\dot{x} = f(x)$ **is called monotone if**

$$a \leq b \implies x(t,a) \leq x(t,b) \text{ for all } t \geq 0.$$

In other words, the flow preserves the partial ordering between the initial conditions for all time $t \geq 0$.

When is a System Monotone?

Definition: **A matrix $A \in R^{nxn}$ is called Metzler if every off-diagonal entry of A is non-negative.**

For example,

$$A = \begin{pmatrix} * & 2 & 0 \\ 2.3 & * & 0 \\ 1 & 4 & * \end{pmatrix}$$

is Metzler.

When is a System Monotone?

Theorem (Kamke, 1932) Consider the system

$$\dot{x} = f(x)$$

whose trajectories evolve on a convex set D.

Let

$$J(x) := \frac{\partial f(x)}{\partial x} \in R^{n \times n}.$$

If $J(x)$ is Metzler for all $x \in D$ then the system is monotone.

Interpretation of Kamke's Condition

The condition:

$$J(x) := \frac{\partial f}{\partial x}(x)$$

is Metzler means that for any $i \neq j$,

$$\frac{\partial f_i}{\partial x_j}(x) \geq 0.$$

Thus, an increase in x_j **yields an increase in** $\dot{x}_i = f_i$.

The state-variables "cooperate" with one another.

Proof of Kamke's Theorem

If **not** **monotone then** $a \le b \nRightarrow x(t,a) \le x(t,b)$ **for all** $t \ge 0$.

This means:

$$x_1(T,a) = x_1(T,b), \quad \textbf{and} \quad x_1(T^+,a) > x_1(T^+,b).$$
$$x_2(T,a) \le x_2(T,b),$$
$$\vdots$$
$$x_n(T,a) \le x_n(T,b),$$

Consider:

$$\dot{x}_1(T,a) - \dot{x}_1(T,b) = f_1\big(x(T,a)\big) - f_1\big(x(T,b)\big)$$
$$= f_1\Big(x(T,b) + \big(x(T,a) - x(T,b)\big)r\Big)\Big|_{r=0}^{r=1}$$
$$= \int_0^1 \frac{\partial f_1}{\partial r}\Big(x(T,b) + \big(x(T,a) - x(T,b)\big)r\Big)dr$$
$$= \int_0^1 \sum_{i=1}^n \left(\frac{\partial f_1}{\partial x_i}(\circ)\right) \big(x_i(T,a) - x_i(T,b)\big)dr$$
$$= \int_0^1 \sum_{i=2}^n \left(\frac{\partial f_1}{\partial x_i}(\circ)\right) \big(x_i(T,a) - x_i(T,b)\big)dr$$
$$\le 0.$$

A Special Case: Positive Linear Systems

Corollary **Consider the linear system:**

$$\dot{x} = Ax, \quad A \text{ Metzler.}$$

Then

$$0 \le b \implies x(t,0) \le x(t,b), \quad \text{that is,}$$

$$0 \le b \implies 0 \le x(t,b) \quad \text{for all} \quad t \ge 0.$$

All the results described below hold for this special case.

Implications of Monotonicity

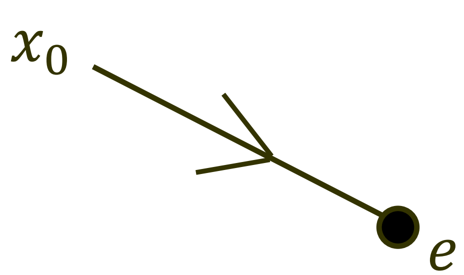
Consider the dynamical system:

$$\dot{x} = f(x)$$

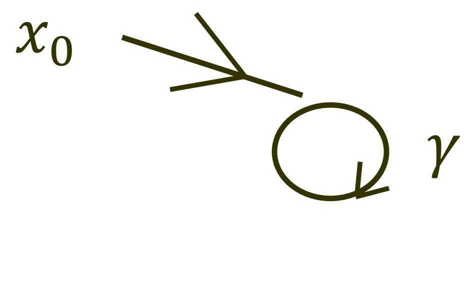
whose trajectories evolve on a compact set D.

Definition: The omega limit set $\omega(x_0)$ **of a point** $x_0 \in D$ **is the set of points** p **such that:**

$$x(t_k, x_0) \to p \text{ for some sequence } t_1, t_2, t_3 \ldots \to \infty.$$



$\omega(x_0) = \{e\}$



$\omega(x_0) = \gamma$

Implications of Monotonicity

Consider the monotone system:

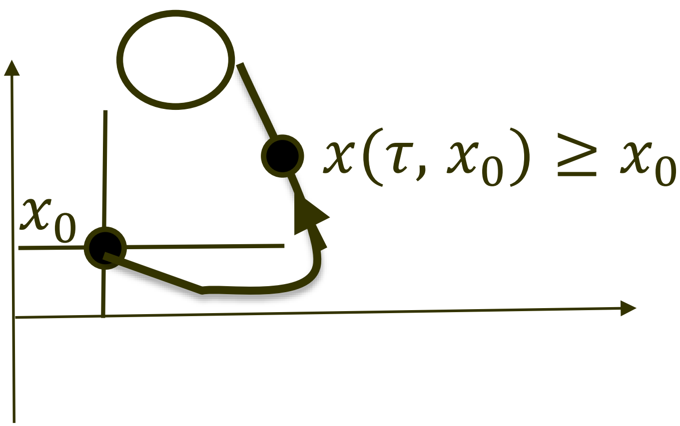
$$\dot{x} = f(x)$$

whose trajectories evolve on a compact set D.

Lemma Pick $x_0 \in D$. **If there exists** $\tau > 0$

such that $x(\tau, x_0) \geq x_0$

then $\omega(x_0)$ **is a closed orbit with period** τ.



Implications of Monotonicity

Lemma **Pick $x_0 \in D$. If there exists $\tau > 0$ such that**

$$x(\tau, x_0) \geq x_0$$

then $\omega(x_0)$ is a closed orbit with period τ.

Sketch of Proof

$$x(\tau, x_0) \geq x_0$$
$$\downarrow$$
$$x(\tau, x(\tau, x_0)) \geq x(\tau, x_0)$$
$$\downarrow$$
$$x(2\tau, x_0) \geq x(\tau, x_0)$$

$$\ldots \geq x(3\tau, x_0) \geq x(2\tau, x_0) \geq x(\tau, x_0) \geq x_0$$

so, $x(k\tau, x_0) \to p \in \omega(x_0)$.

Implications of Monotonicity

Theorem (Hirsch, 1988) **Almost every compact trajectory of a monotone system converges to the set of equilibria.**

Two results that provide more information, under additional assumptions, are:

1. **Ji-Fa's Theorem**
2. **Smillie's Theorem**

Ji-Fa's Theorem (1994)

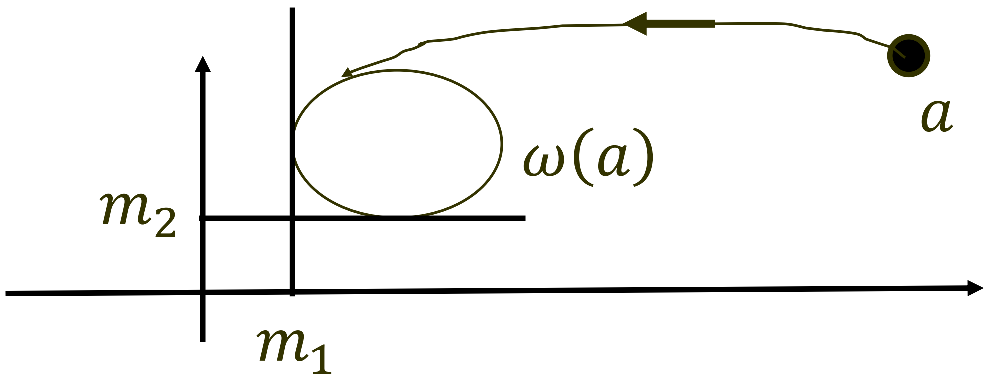
Theorem **Consider the monotone system:**

$$\dot{x} = f(x)$$

whose trajectories evolve on a compact set D**.**
If D **contains a single equilibrium point** e **then**

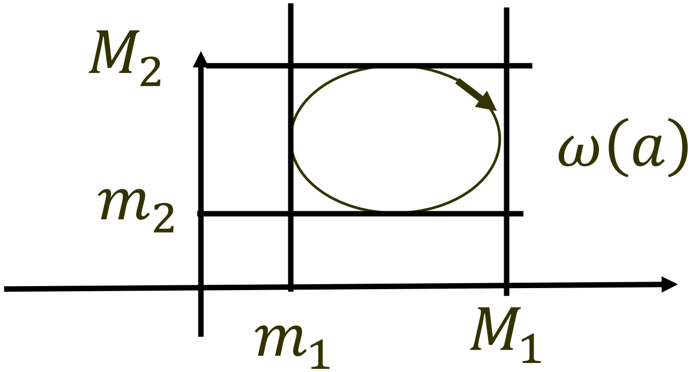
$$\lim_{t\to\infty} x(t,a) = e \quad \textbf{for all} \quad a \in D.$$

Proof **Pick** $a \in D$. **Let** $m := \inf(\omega(a))$.



Ji-Fa's Theorem-Sketch of Proof

Pick $a \in D$. **Let** $m := \inf(\omega(a)), M := \sup(\omega(a))$.



Ji-Fa showed: $x(t,m) \leq m,\ x(t,m) \to e$.

and, similarly, $x(t,M) \geq M,\ x(t,M) \to e$.

Thus, $x(t,m) \leq m \leq \omega(a) \leq M \leq x(t,M)$.

$$\downarrow \qquad\qquad\qquad\qquad \downarrow$$
$$e \qquad\qquad\qquad\qquad e$$

So, $\omega(a) = \{e\}$.

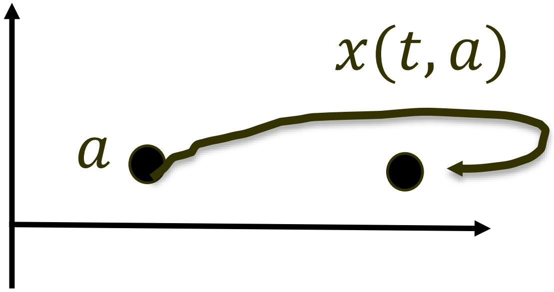
Smillie's Theorem (1984)

Theorem **Consider the monotone system:**

$$\dot{x} = f(x)$$

whose trajectories evolve on a compact set D. If $J(x)$ is tridiagonal and strongly Metzler on D then $x(t,a)$ converges to an equilibrium for all $a \in D$.

$$J(x) = \begin{pmatrix} * & + & 0 & 0 \\ + & * & + & 0 \\ 0 & + & * & + \\ 0 & 0 & + & * \end{pmatrix}$$



Smillie's Theorem (1984)

Idea of Proof **For** $y \in R^n$, **let** $\sigma(y)$ **be the number of sign changes in** y:

$$\sigma\begin{pmatrix}1\\-2\\4.17\end{pmatrix}=2.$$

Let $z(t) := \dot{x}(t) = f(x(t))$. **Then**

$$\dot{z}(t) = J\big(x(t)\big)\dot{x}(t) = J\big(x(t)\big)z(t).$$

Smillie showed: $\sigma\big(\mathrm{z}(\mathrm{t})\big)$ **is non-increasing in** t.

Since this function is bounded below by zero, it can be used as a discrete-valued Lyapunov function.

Smillie's Theorem (1984)

Idea of Proof **analyzing sign changes in** $z(t) \coloneqq \dot{x}(t)$.

Seeking a contradiction, assume:

$z(t^-)$	$z(t)$	$z(t^+)$
$+$	$+$	$+$
$+$	0	$-$
$+$	$+$	$+$

Then:

$$\dot{z}(t) = J\big(x(t)\big)z(t)$$

$$= \begin{pmatrix} * & + & 0 \\ + & * & + \\ 0 & + & * \end{pmatrix} \begin{pmatrix} + \\ 0 \\ + \end{pmatrix}$$

$$= \begin{pmatrix} * \\ + \\ * \end{pmatrix}.$$

Application 1: the Ribosome Flow Model (RFM)

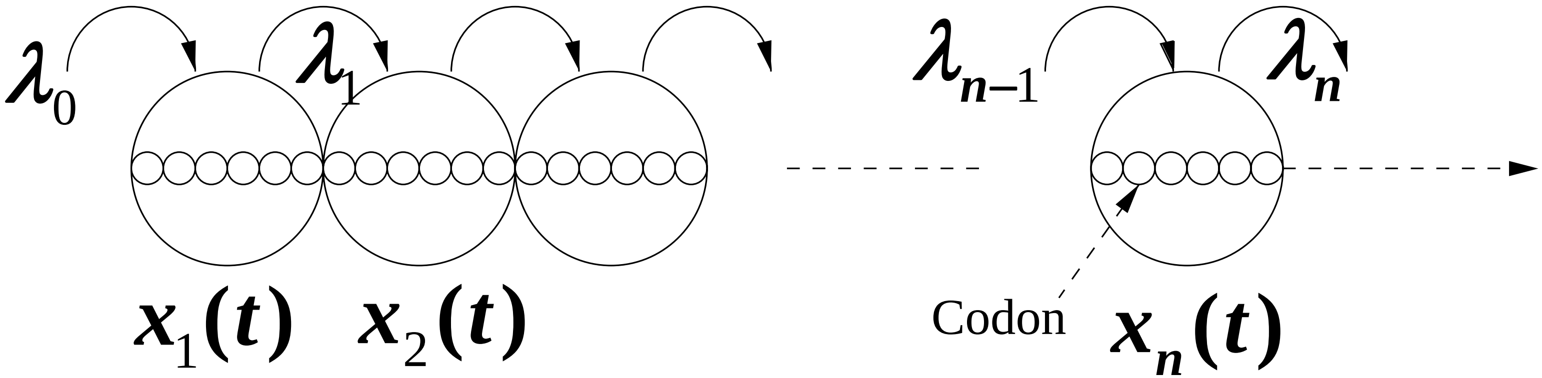
Biological "machines" that move along a lattice of sites:

- **Ribosome flow along the mRNA molecule**
- **Molecular motors move cargo along microtubules**

The "machines" have volume leading to simple exclusion.

The Ribosome Flow Model (RFM) allows modeling and analyzing such processes.

Ribosome Flow Model



$x_1(t)=0$ **site 1 is completely free;**

$x_1(t)=1$ **site 1 is completely full**

$$\dot{x}_1 = \lambda_0(1-x_1) - \lambda_1 x_1(1-x_2)$$

$$\dot{x}_2 = \lambda_1 x_1(1-x_2) - \lambda_2 x_2(1-x_3)$$

$$\vdots$$

$$\dot{x}_n = \lambda_{n-1} x_{n-1}(1-x_n) - \lambda_n x_n$$

Ribosome Flow Model*

$$\dot{x}_1 = \lambda_0(1 - x_1) - \lambda_1 x_1(1 - x_2)$$

$$\dot{x}_2 = \lambda_1 x_1(1 - x_2) - \lambda_2 x_2(1 - x_3)$$

$$\vdots$$

$$\dot{x}_n = \lambda_{n-1} x_{n-1}(1 - x_n) - \lambda_n x_n$$

unidirectional movement & simple exclusion

$R(t) := \lambda_n x_n(t)$ **is the translation rate at time** t**.**

*Reuveni, Meilijson, Kupiec, Ruppin & Tuller, "Genome-scale Analysis of Translation Elongation with a Ribosome Flow Model", *PLoS Comput. Biol.*, 2011

The RFM is Monotone

$$\dot{x}_1 = \lambda_0(1 - x_1) - \lambda_1 x_1(1 - x_2),$$
$$\dot{x}_2 = \lambda_1 x_1(1 - x_2) - \lambda_2 x_2(1 - x_3),$$
$$\dot{x}_3 = \lambda_2 x_2(1 - x_3) - \lambda_3 x_3.$$

Jacobian:

$$J(x) = \begin{pmatrix} * & \lambda_1 x_1 & 0 \\ \lambda_1(1 - x_2) & * & \lambda_2 x_2 \\ 0 & \lambda_2(1 - x_3) & * \end{pmatrix}$$

and this is Metzler on $[0,1]^3$.

RFM is Monotone: Explanation

$$\dot{x}_1 = \lambda_0(1 - x_1) - \lambda_1 x_1(1 - x_2),$$
$$\dot{x}_2 = \lambda_1 x_1(1 - x_2) - \lambda_2 x_2(1 - x_3),$$
$$\dot{x}_3 = \lambda_2 x_2(1 - x_3) - \lambda_3 x_3.$$

Consider:

$$\dot{x}_2 = \lambda_1 x_1(1 - x_2) - \lambda_2 x_2(1 - x_3),$$

This increases with the density at site 1 and with the density at site 3.

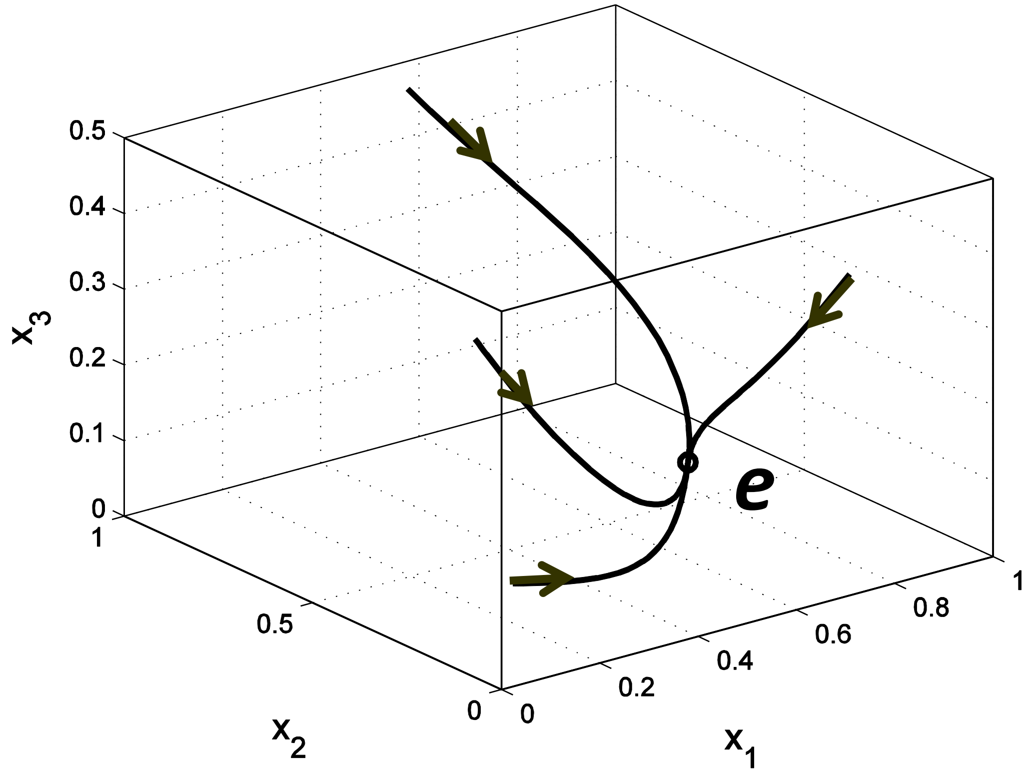
Application to the RFM

Corollary 1: **All trajectories of the RFM converge to a unique equilibrium point *e*.***

Biological interpretation: **the parameters determine a unique steady-state of ribosome distributions and protein production rate.**

*Margaliot and Tuller, “Stability Analysis of the Ribosome Flow Model”, *IEEE TCBB,* 2012.

Simulation Results



All trajectories emanating from *C:=[0,1]³* remain in *C*, and converge to a unique equilibrium point *e*.

Application 2: A Model from Electrophysiology*

- **Cells are electrically coupled into networks via gap junctions (plaques of ion channels).**
- **Passage of ions across the junction is diffusive, and depends linearly on the voltage difference across the junction.**

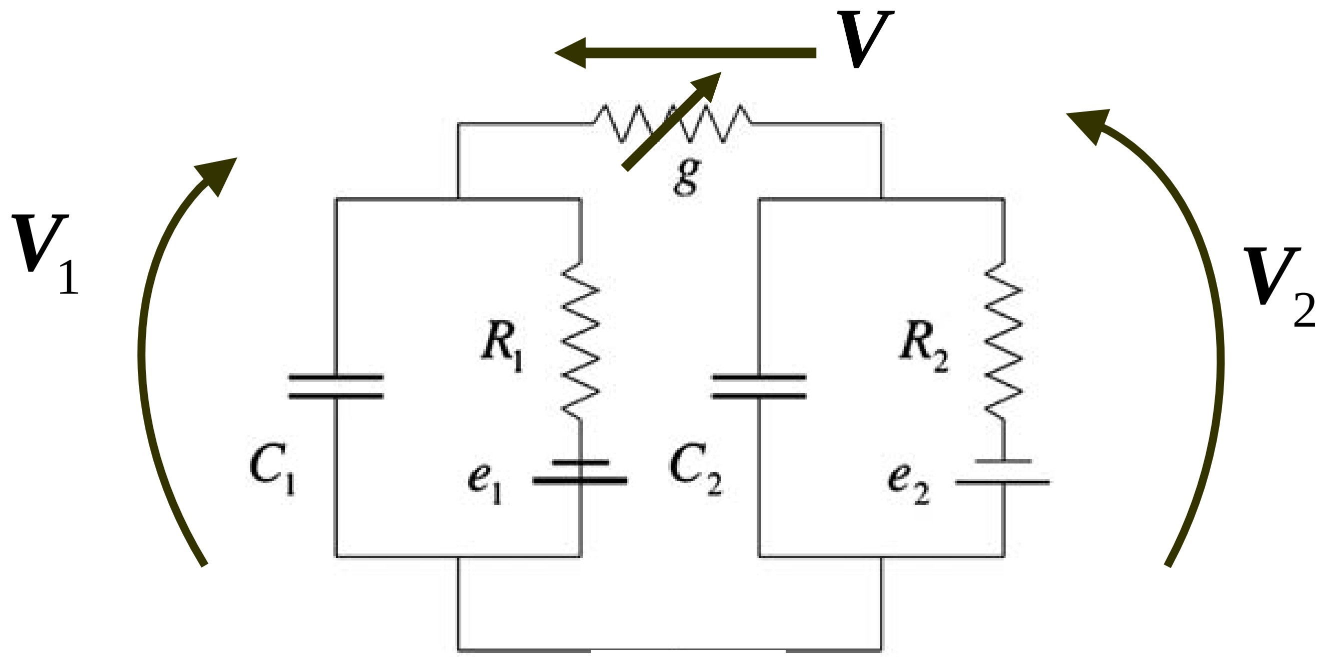
*Donnell, Baigent & M. Banaji, “Monotone dynamics of two cells dynamically coupled by a voltage-dependent gap junction”, *JTB*, 2009.

Application 2: A Model from Electrophysiology

- **Isolated cells typically oscillate. What happens when they are connected via gap junctions?**
- **Analytically tractable model of two cells electrically coupled via a dynamic gap junction, and proof of convergence using Smillie's theorem.**

*Donnell, Baigent & M. Banaji, "Monotone dynamics of two cells dynamically coupled by a voltage-dependent gap junction", *JTB*, 2009.

A Model from Electrophysiology



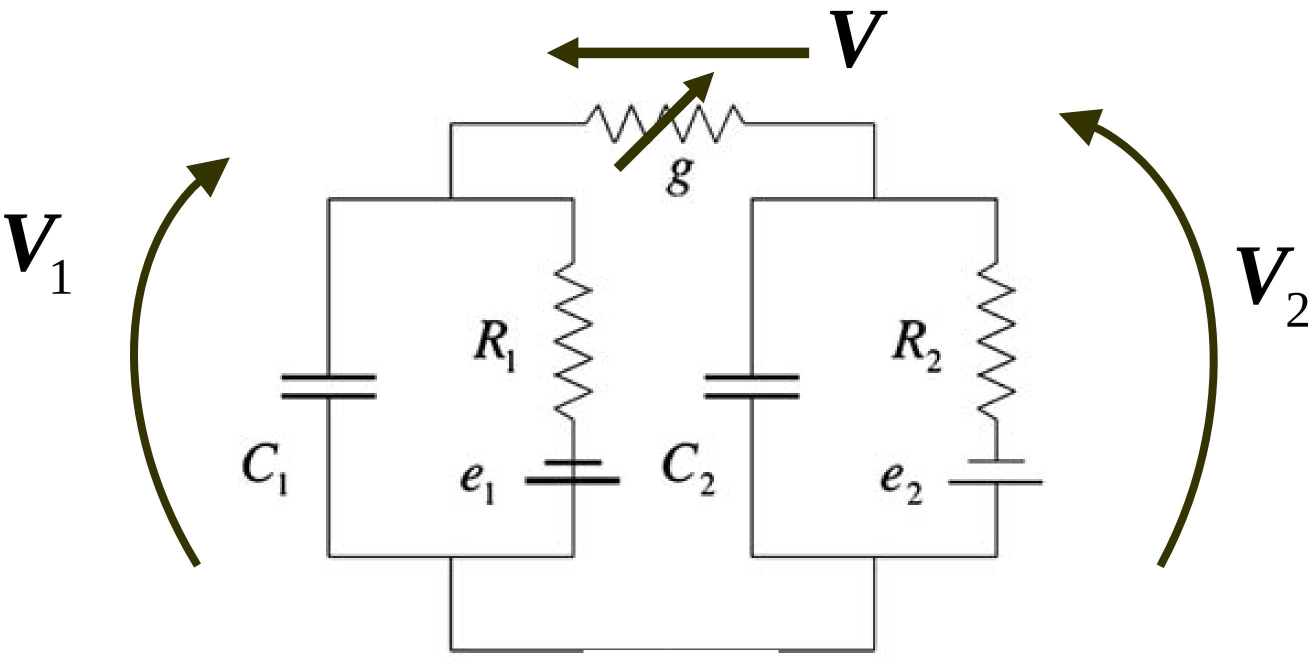
e_i - cell resting potential.

$x(t)$ - fraction of gap channels that are open.

$$\dot{x} = -\alpha(\mathrm{V})x + \beta(V)(1-x), \quad \mathrm{V}\,\alpha'(\mathrm{V}), \mathrm{V}\,\beta'(\mathrm{V}) > 0.$$

$$g(\mathbf{x}(t)) = x(t)g_{\min} + (1-x(t))g_{\max}.$$

A Model from Electrophysiology

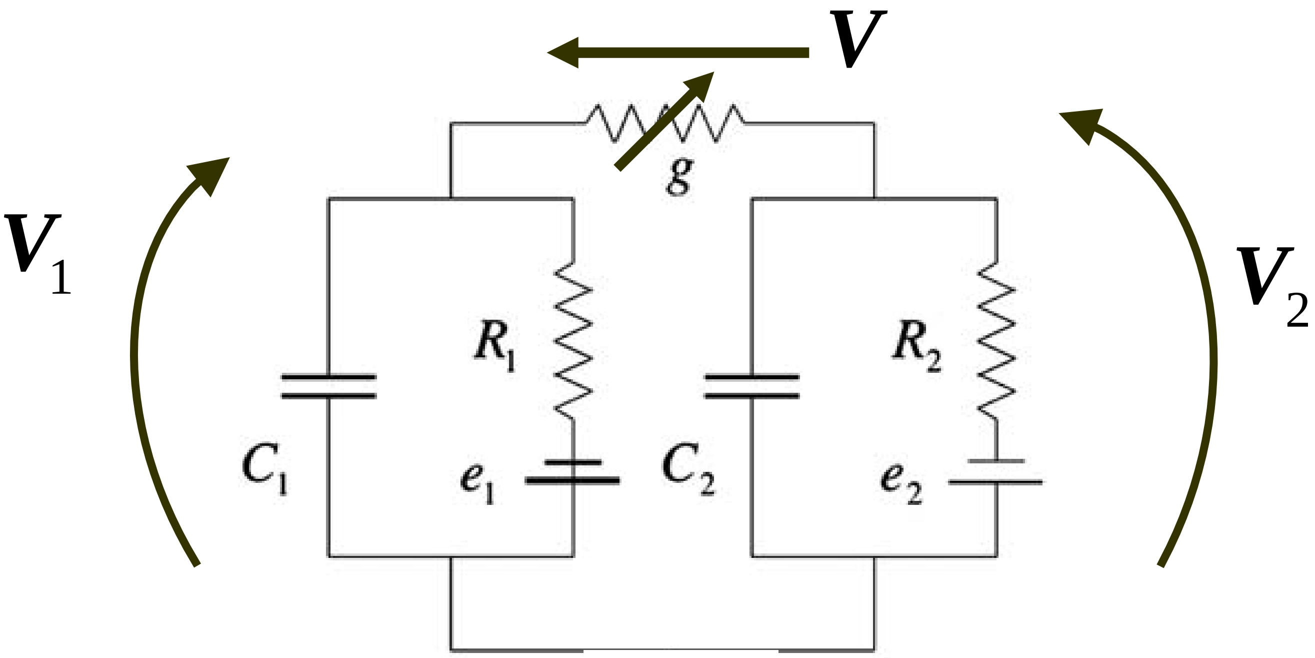


$$C_1\dot{V}_1 = -(1/R_1)(V_1 - e_1) - (V_1 - V_2)\,\mathbf{g}(\mathbf{x}),$$

$$C_2\dot{V}_2 = -(1/R_2)(V_2 - e_2) + (V_1 - V_2)\,\mathbf{g}(\mathbf{x}),$$

$$\dot{\mathbf{x}} = -\alpha(V_1 - V_2)\,\mathbf{x} + \beta(V_1 - V_2)(1 - \mathbf{x}).$$

A Model from Electrophysiology

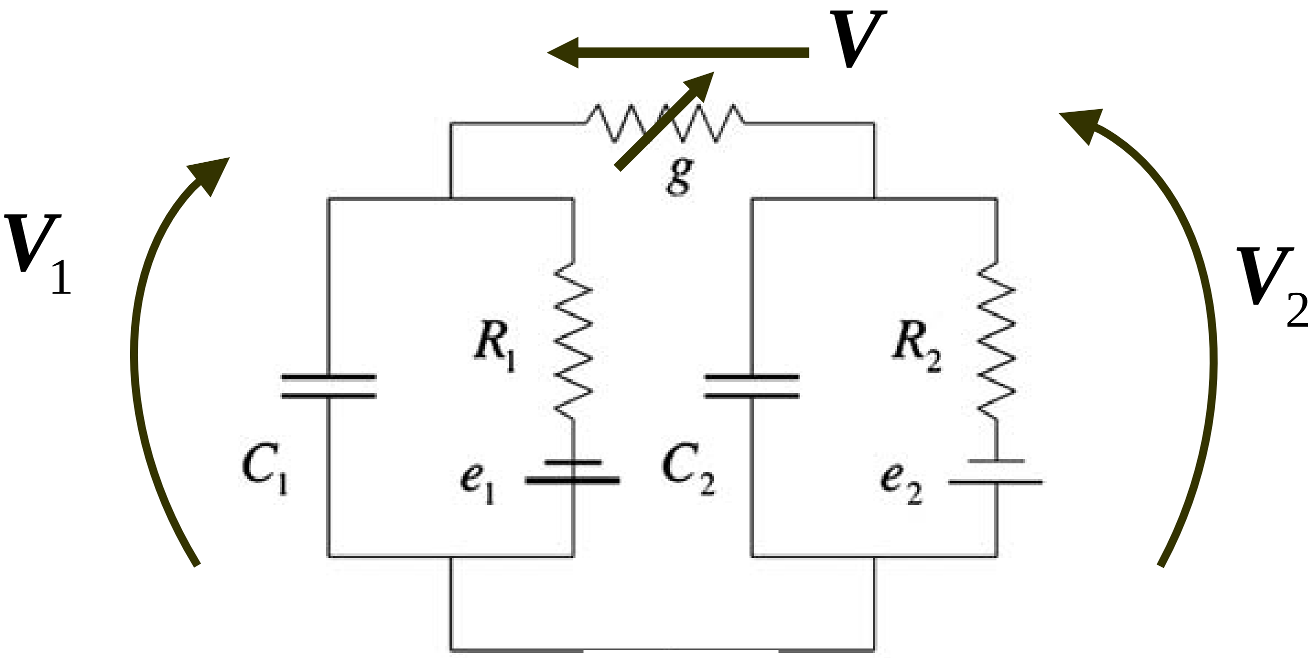


In the transformed state-variables,

$$x,\ V,\ \Psi := C_1V_1 + C_2V_2,$$

$$J = \begin{pmatrix} * & + & 0 \\ + & * & + \\ 0 & + & * \end{pmatrix}$$

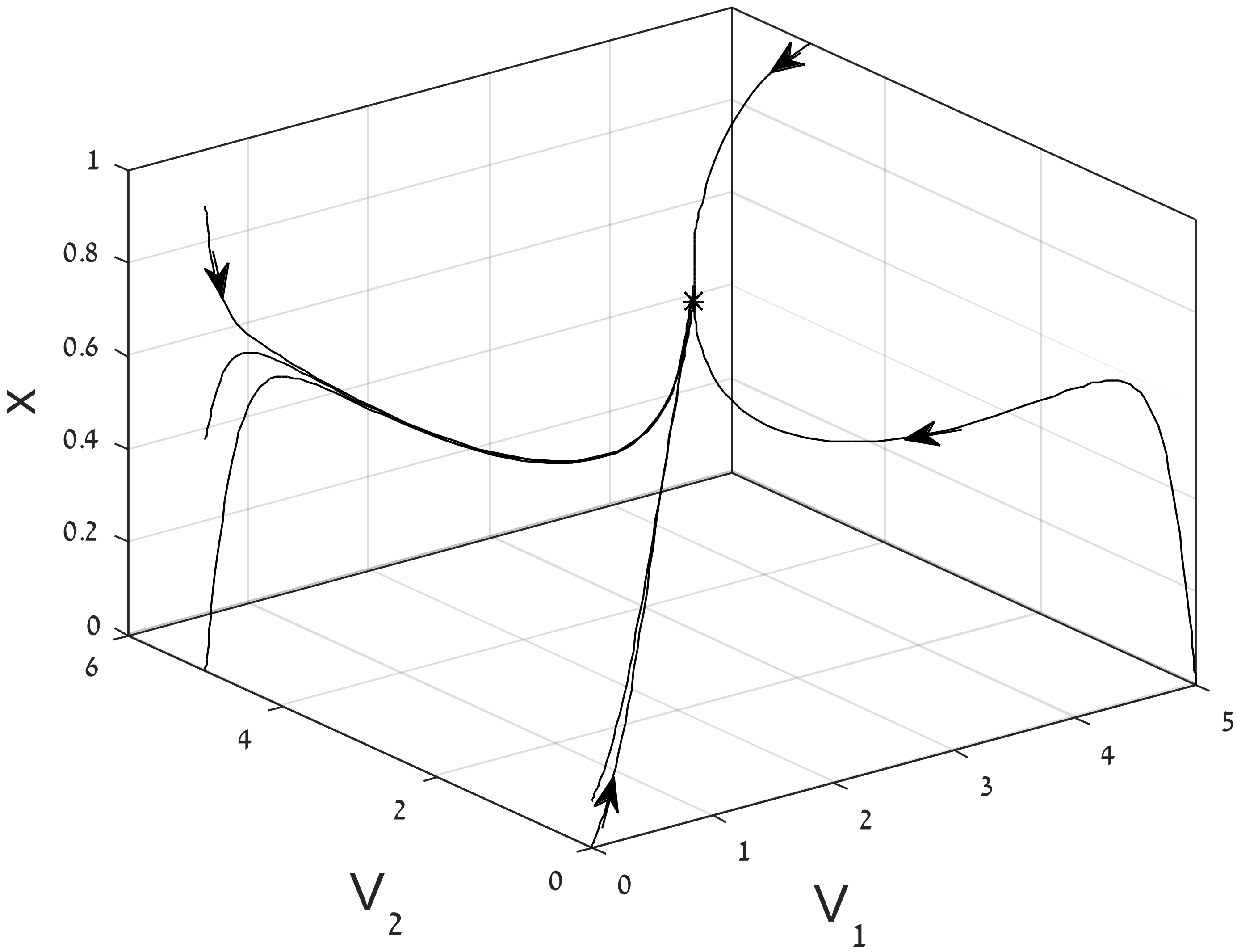
A Model from Electrophysiology



$$J = \begin{pmatrix} * & + & 0 \\ + & * & + \\ 0 & + & * \end{pmatrix}$$

By Smillie's theorem, every solution converges to an equilibrium.

Simulation



Conclusions

Monotone dynamical systems enjoy a deep and powerful theory and have found numerous applications in various fields.

We only discussed ODEs.

Many of the results hold for:

--Infinite-dimensional systems;

--PDEs;

--Systems with time-delay,….

Further Reading

- **H. L. Smith, Monotone Dynamical Systems, 2008.**
- **D. Angeli & E. D. Sontag, Monotone control systems, IEEE TAC, 2003.**

THANK YOU!

Additional Slides

```
function ret=banaji_dyn(t,y)

v1=y(1);v2=y(2);x=y(3);
C1=1;C2=1/2;R1=1;R2=5;e1=2;e2=1;
g=x*1/2+(1-x)*2;
ret1=(-(1/R1)*(v1-e1)-(v1-v2)*g)/C1;
ret2=(-(1/R2)*(v1-e2)+(v1-v2)*g)/C2;
ret3=-(v1-v2)^2*x+cosh((v1-v2))*(1-x);
ret=[ret1;ret2;ret3];
----------------------------------------
Eq=[1.8333    1.6001    0.8571]
```