Delays and Dynamics in Models of Neural Activity

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Models

1. Biological neuron models

   - Hodgkin-Huxley (1952) – Four coupled ODEs
   - FitzHugh–Nagumo (1961) – Reduced model, two ODEs
   - Morris–Lecar (1981)
   - Hindmarsh–Rose (1984)
   - Rulkov map (2001)

2. Networks: Connections are important!

   - Leaky integrate-and-fire neurons

$$\dot{V}_i(t) + V_i(t) = S\left(\sum_{j=1}^{n} a_{ij} V_j(t)\right), \quad i = 1, 2, \ldots, n.$$

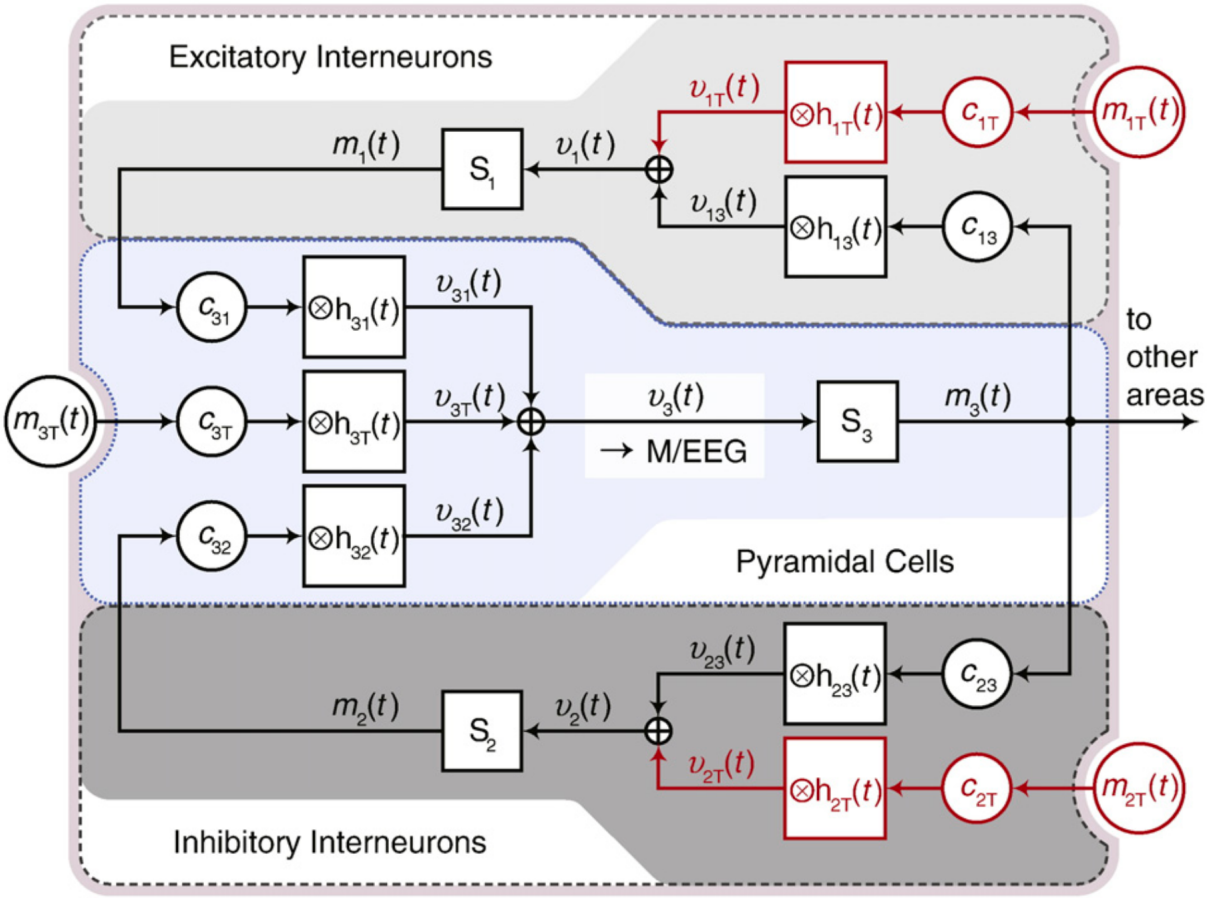
3. Networks of networks

4. Emergence: The whole is more than the sum of its parts

Outline

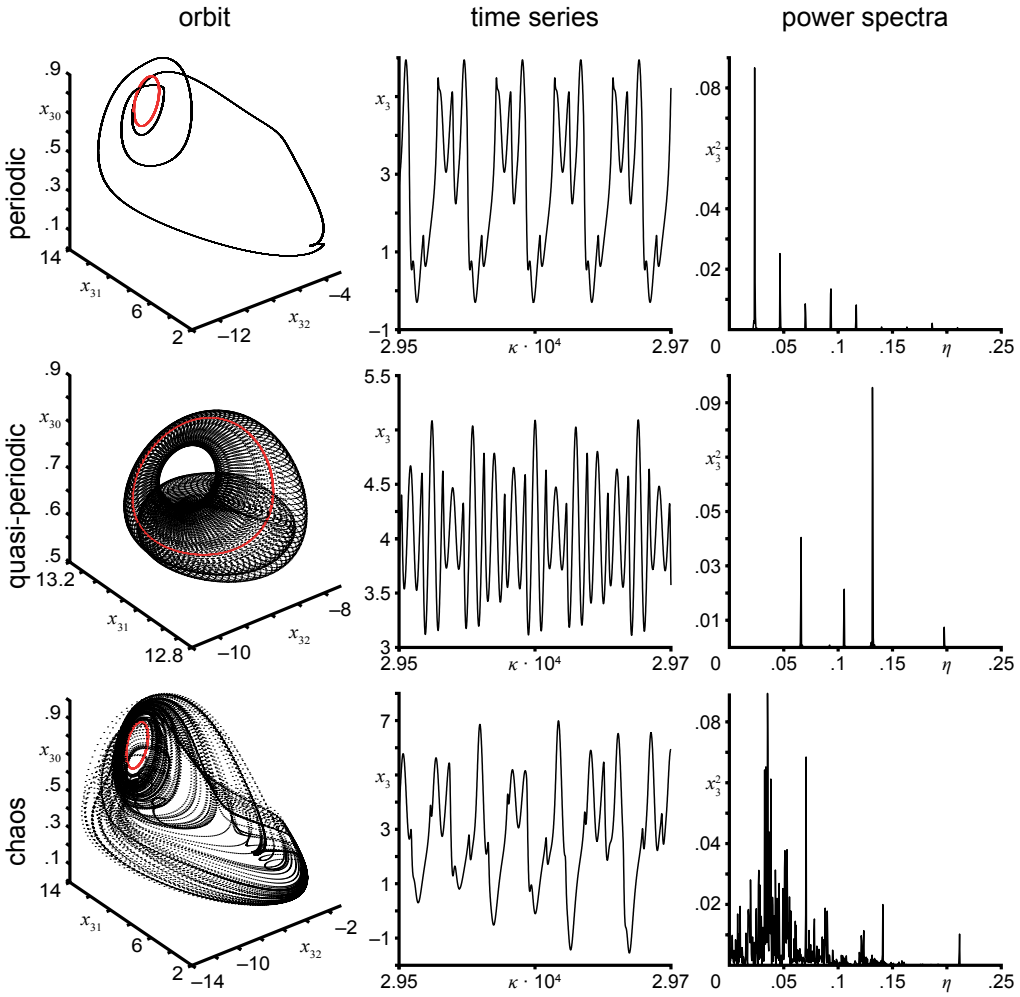
- Brain dynamics
  - Activity (oscillations)
  - Spread of activity (traveling waves,...)
  - Collective behavior (synchronization,...)
- Biological models and delays
  - Individual neurons
  - Locally averaged and homogenized representations (Neural fields)
  - Lumped systems (Neural mass models)
- Tools for studying emergence
  - Local bifurcations
  - Global phenomena

Neural Mass Models – Ignoring space dimension



(Jansen & Rit, Biol. Cybern. 1995)

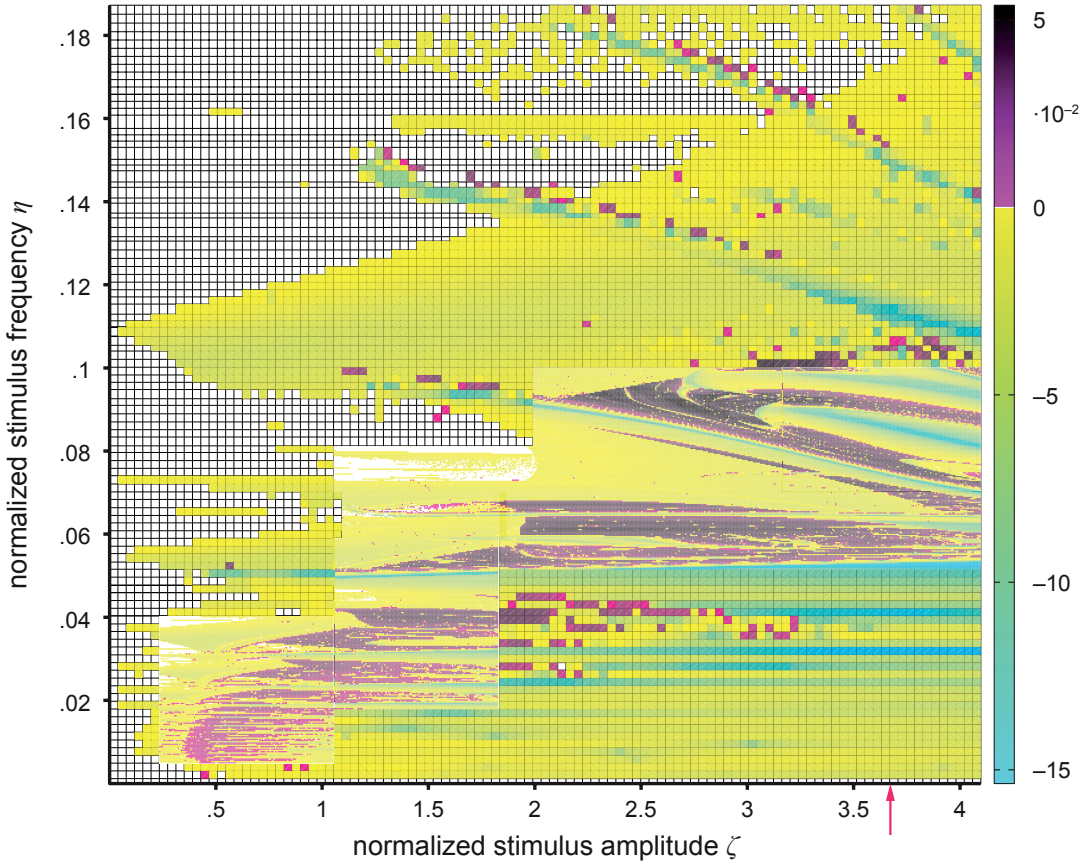
Dynamics and bifurcations in neural mass models



Bifurcation analysis: Spiegler et al., Neuroimage 2010.

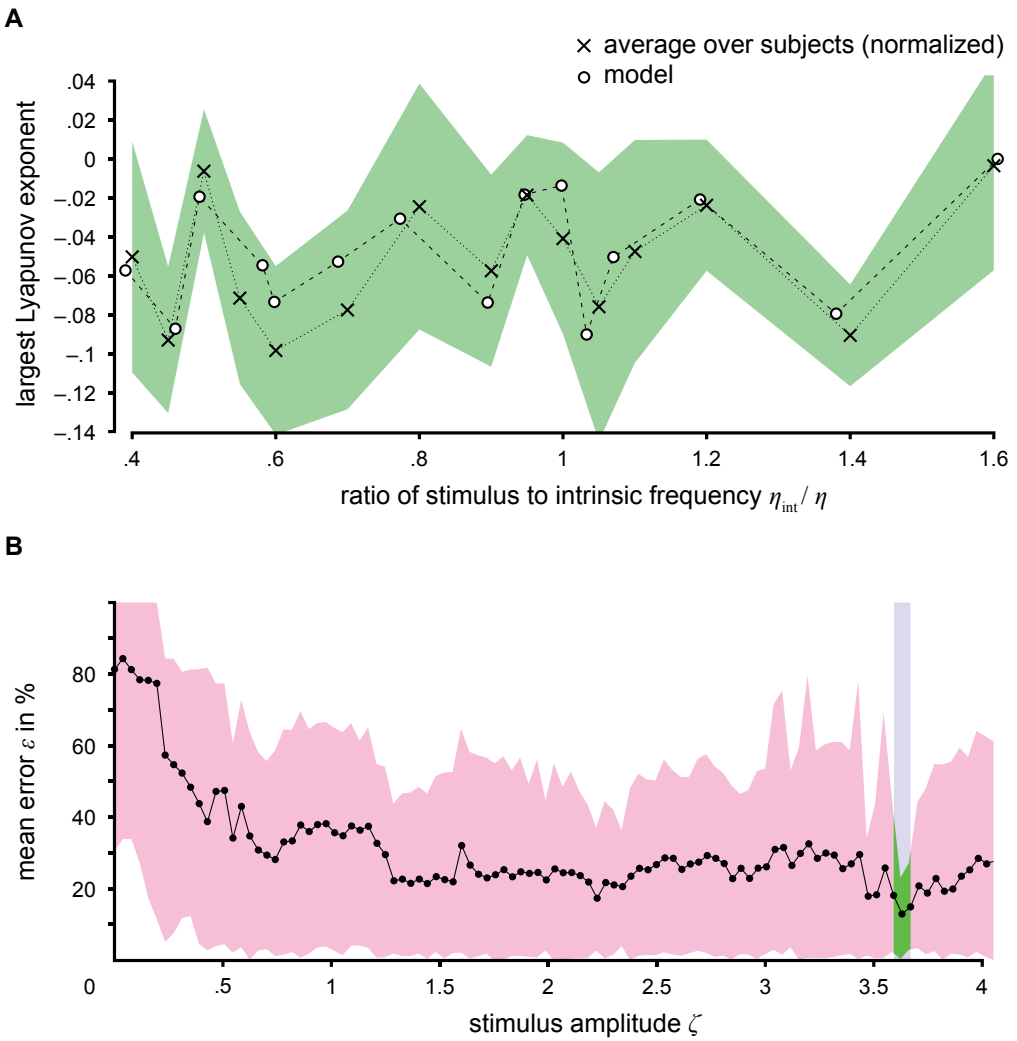
Lyapunov exponents in photic driving experiment

Photic driving: Stimulation by repetitive light flashes entrains the intrinsic alpha EEG rhythm and is widely used as an activation method in clinical practice, e.g., in epilepsy, migraine, schizophrenia, or depression.



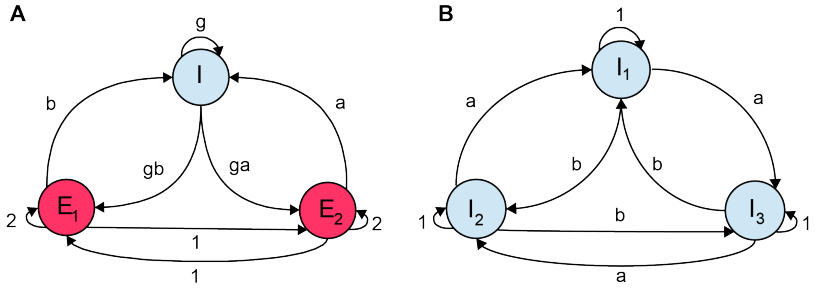
(Spiegler et al., PLoS Comp. Biol. 2011)

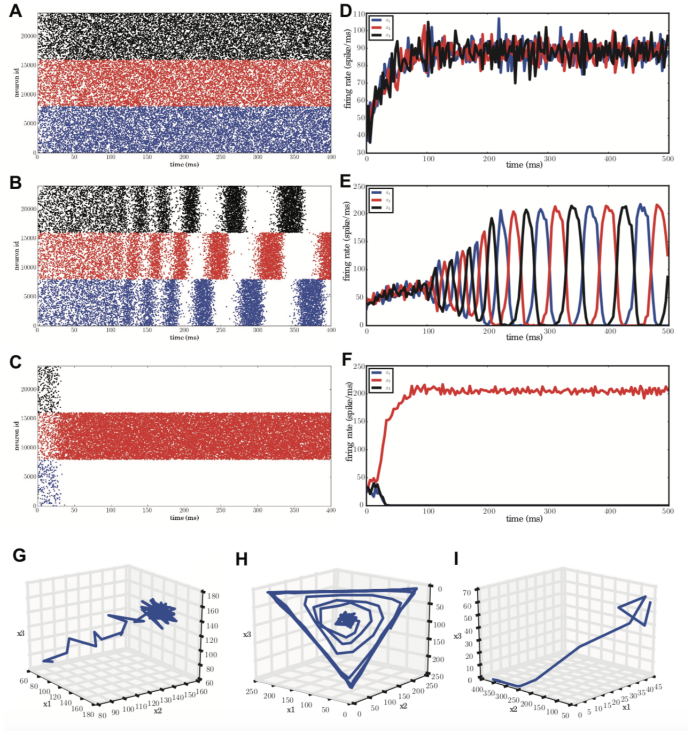
Fit to experimental data



(Spiegler et al., PLoS Comp. Biol. 2011)

Bifurcation analysis of networks of a spiking networks





(Lagzi, FA, & Rotter, Scientific Reports 2019)

Time delays

Nothing is inevitable but death and taxes. (B. Franklin)

Delays are also inevitable. (A. Einstein)

- Nothing (mass/energy/information) in the universe can travel faster than $c = 299{,}792{,}458$ m/sec.
- *Every* spatially extended system has delays.
- Neural signal propagation along axons $\sim 0.1 - 10$ m/sec.
- Delays in neuro-muscular reflex loops ~ 0.1 sec.
- Usually significant, since relevant time scale in neural networks ~ 1 ms

Neuronal ensembles and field models – Time delays over space

- Neurons have large spatial density, $\sim 10^4$ neurons/mm^3
- Consider ensemble activity on a larger spatial scale, say, > 1 mm (Wilson & Cowan 1973)

Coarse-grained activity of neural ensembles

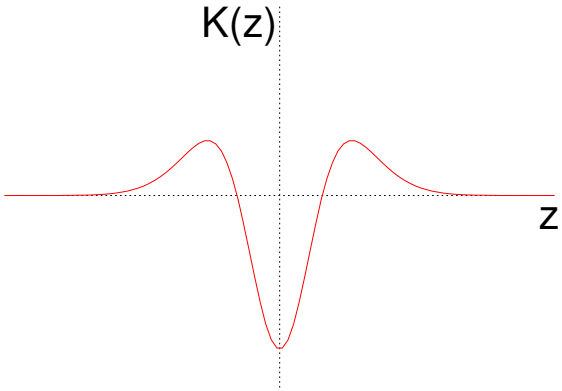
$$\mathcal{D}(\partial/\partial t)V(x,t) = \alpha \int_\Omega K(|x-y|)S\left(V\left(y, t - \frac{|x-y|}{v}\right)\right) dy + E(x,t)$$

V : mean postsynaptic potential
Ω : spatial domain
K : connectivity kernel
S : sigmoidal transfer function
v : axonal transmission speed
E : external input
$\mathcal{D}$: temporal differential operator (usually 1st or 2nd order)

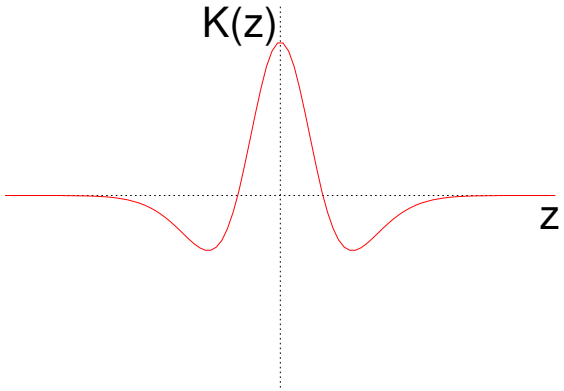
- Propagation delay: $|x-y|/v$

Field connectivity

Local inhibition-
lateral excitation



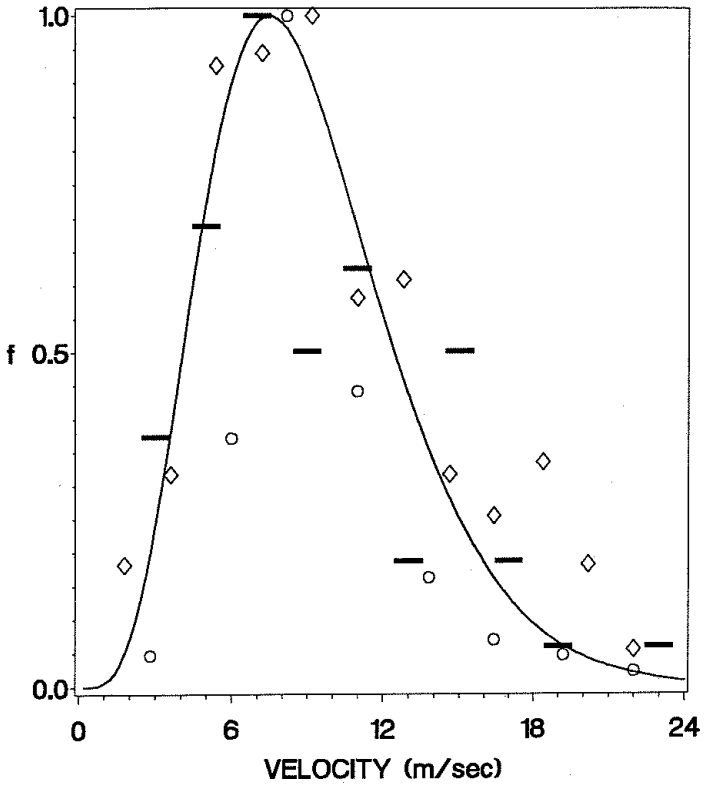
Local excitation-
lateral inhibition



- Can have different connectivities and signal speeds for inhibitory and excitatory neurons. (Hutt & FA, PhysicaD 2005)
- Precise connections unknown in the brain.
- What can we say about the dynamics for general connectivity?

Propagation speed distributions

Myelinated corticocortical fibers, experimental data (Nunez 1995, Katznelson 1981.)



Also in intracortical connections in visual cortex of cats and monkeys (Bringuier et al., Science 1999; Eckhorn et al. IEEE Trans. Neur. Net. 2004)

Neural field model

Coarse-grained activity of neural ensembles:

$$\mathcal{D}(\partial/\partial t)V(x,t) = \alpha \int_0^\infty g(v) \int_\Omega K(|x-y|) S\left(V\left(y, t - \frac{|x-y|}{v}\right)\right) dy\, dv + E(x,t)$$

- Distribution of propagation velocities $g(v)$

V : mean postsynaptic potential $\quad \Omega$: spatial domain
K : connectivity kernel $\quad S$: sigmoidal transfer function
v : axonal transmission speed $\quad E$: external input
$\mathcal{D}$: temporal differential operator (usually 1st or 2nd order)

Nonlocal feedback

- Feedback loops important in real neural processing (e.g. cortico-thalamic loops).
- Experimental findings indicate a network of interacting neural areas (Salinas & Senjowski 2001), which allows the brain to accomplish complex tasks like motor-coordination or visual feature binding (Singer & Gray 1995) .
- Introduce general non-local feedback kernels and delay distributions into the model.

Neural field model

Coarse-grained activity of neural ensembles:

$$\mathcal{D}(\partial/\partial t)V(x,t) = \alpha \int_0^\infty g(v) \int_\Omega K(|x-y|) S\left(V\left(y, t - \frac{|x-y|}{v}\right)\right) dy\, dv + E(x,t)$$
$$+\beta \int_0^\infty f(\tau) \int_\Omega F(|x-y|) S(V(y, t-\tau))\, dy\, d\tau$$

- Nonlocal connectivity F.
- Nonlocal feedback delay τ with distribution f.

(FA & Hutt, SIAM J. Appl. Dyn. Syst. 2006)

Dynamics: Stability of equilibria

Find equilibria and study their stability as parameters are varied.

- Spatially uniform equilibria $V(x,t) = V^*$ for constant external input.
- Linearize about V^*. Determine the fate of perturbations

$$u(x,t) = e^{\lambda t} e^{ikx}$$

  about V^*.

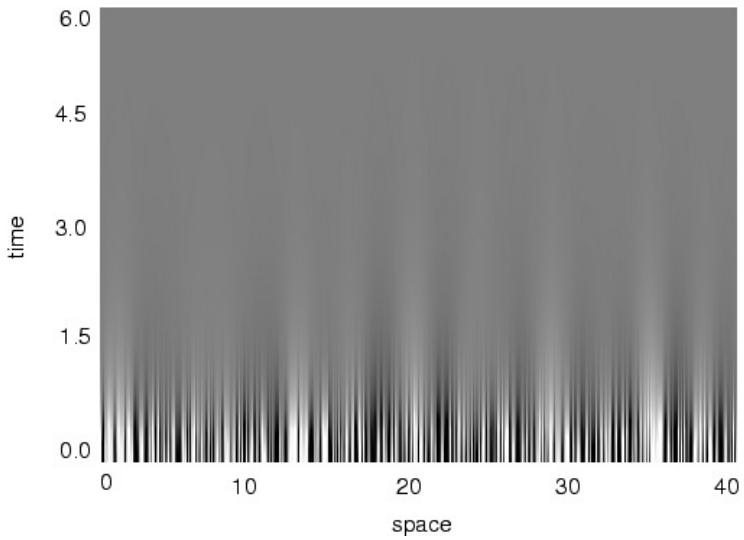
- $\mathrm{Re}\,\lambda < 0 \Rightarrow$ Stability
  $\mathrm{Re}\,\lambda > 0 \Rightarrow$ Instability
  $\mathrm{Re}\,\lambda = 0 \Rightarrow$ Critical value (bifurcation)

Bifurcations of equilibria

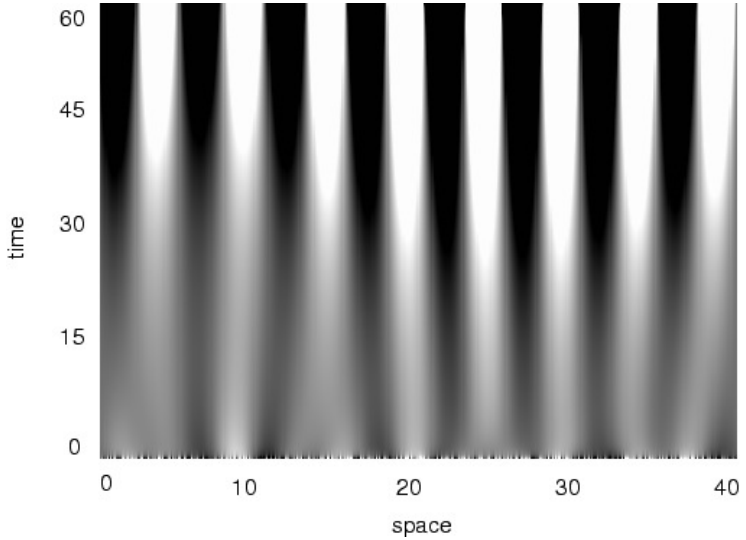
$$u(x,t) = e^{\lambda t} e^{ikx}, \quad \lambda = i\omega, \, \omega \in \mathbb{R}$$

- *Stationary bifurcations*
  - $\omega = 0$ *and* $k = 0 \Rightarrow$ *New equilibrium*
  - $\omega = 0$ *and* $k \neq 0 \Rightarrow$ *Spatial patterns (Turing modes)*
- *Non-stationary bifurcations*
  - $\omega \neq 0$ *and* $k = 0 \Rightarrow$ *Spatially uniform oscillations (synchrony)*
  - $\omega \neq 0$ *and* $k \neq 0 \Rightarrow$ *Traveling waves, wave speed* ω/k.

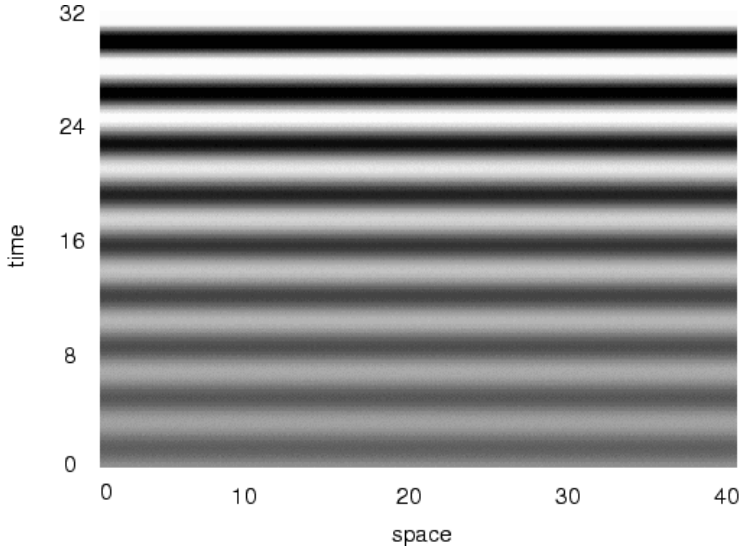
Stable equilibrium



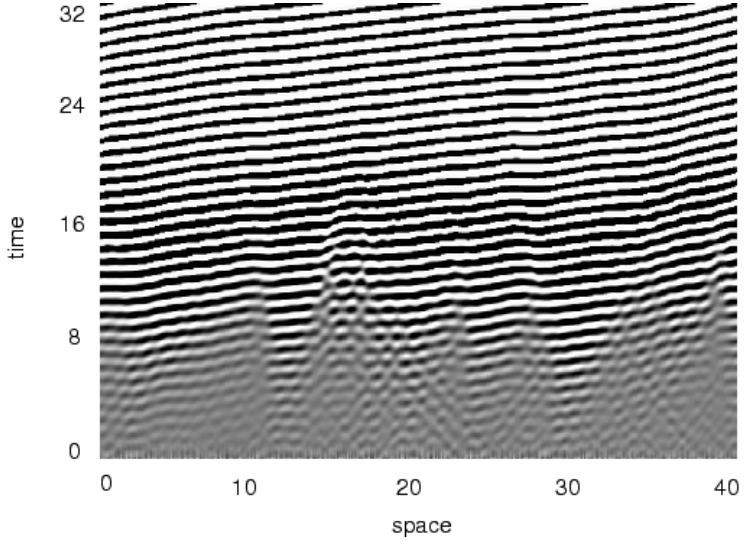
Turing patterns



Uniform oscillations



Traveling waves



Role of delays in bifurcations

Define the characteristic propagation delay

$$\tau_p = \int_0^\infty \frac{g(v)}{v}\, dv \int_{-\infty}^{\infty} |zK(z)|\, dz$$

Theorem 1. *Suppose* $\mathcal{D}(\frac{\partial}{\partial t}) = \eta\frac{\partial^2}{\partial t^2} + \gamma\frac{\partial}{\partial t} + \rho$, *where* $\eta = 0$ *or* 1 *and* $\gamma, \rho \in R$. *If*

$$\alpha\tau_p + \beta E[\tau] < |\gamma|$$

then there are no oscillatory bifurcations of spatially homogeneous equilibria.

- Temporal oscillations can bifurcate *only when* sufficiently large delays are present.

(FA & Hutt, SIAM J. Appl. Math. 2005)

Examples from neural dynamics

- Spatially homogeneous synchronous oscillations (Singer)
- Synfire chains: Propagating volleys of synchronous oscillations (Abeles)

Appearance of such behavior from rest state are intimately connected to time delays.

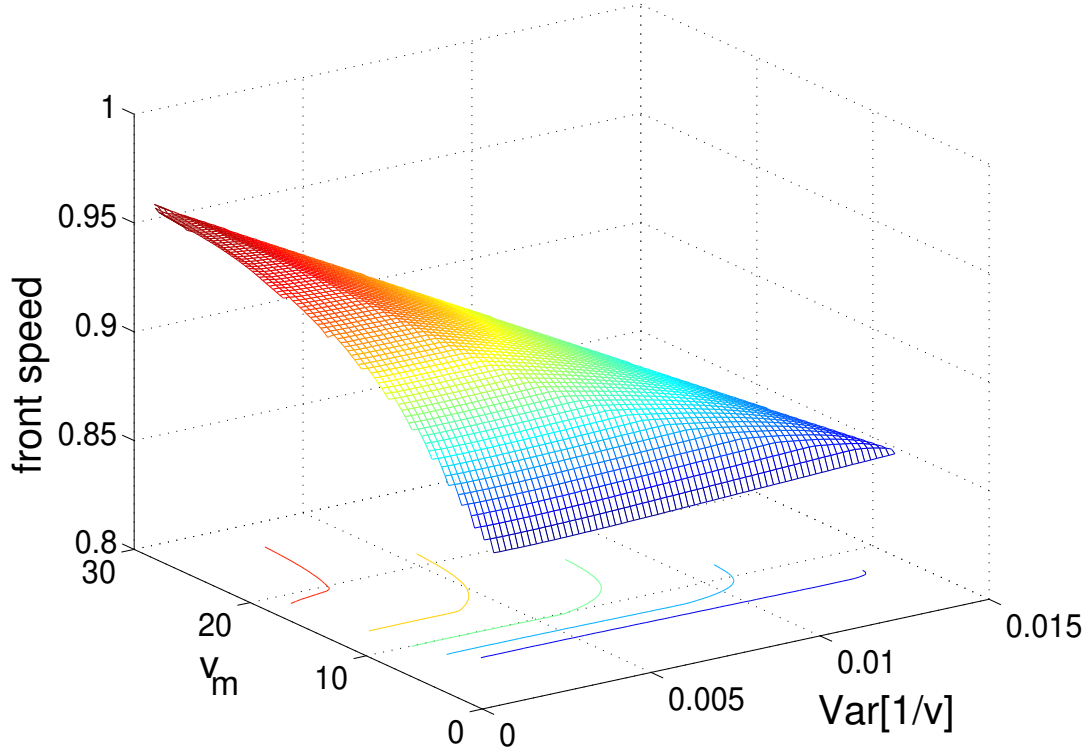
Generic qualitative behavior near equilibria

Dominant mode of bifurcation for a sufficiently general class of connectivity kernels
(FA & Hutt, SIAM J. Appl. Dyn. Syst. 2006)

- In the absence of non-local feedback term
  - Slow signal propagation $\Rightarrow$ Traveling waves
  - Fast signal propagation $\Rightarrow$ Pattern formation
- With non-local feedback
  - Excitatory feedback $\Rightarrow$ Stationary bifurcations
  - Inhibitory feedback $\Rightarrow$ Oscillatory bifurcations
- Highly non-local feedback (high variance of feedback kernel F) favors spatially homogeneous bifurcations
  - Excitatory feedback $\Rightarrow$ Homogeneous equilibria
  - Inhibitory feedback $\Rightarrow$ Homogeneous oscillations (*Synchronization*)
- Bifurcations can be calculated from the first few moments of the connectivity kernel.

Global phenomena: Traveling fronts

Gamma-distributed propagation speeds with mean v_m.



- Shape of propagation speed distribution affects front speed.
  Front speed can be maximized by distributed propagation speeds. (Hutt & FA PRE 2006)

Nonlinear systems and dynamical patterns

- General coupled systems

$$\dot{x}_i(t) = f(x_i(t)) + g_i(x_1(t-\tau), x_2(t-\tau), \ldots, x_n(t-\tau)),$$

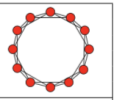
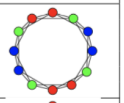
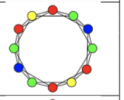
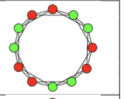
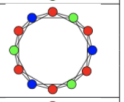
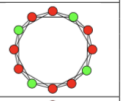
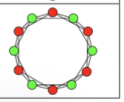
for example, neural network models

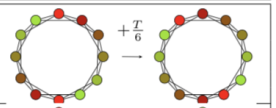
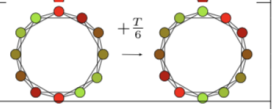
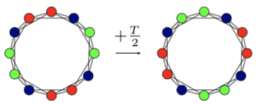
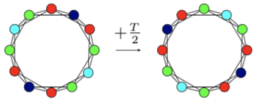
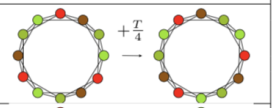
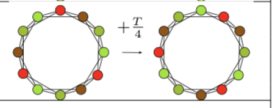
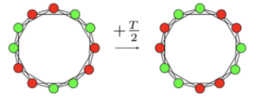
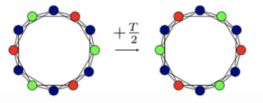
$$\dot{x}_i(t) + x_i(t) = S\left(\sum_{j=1}^{n} a_{ij} x_j(t-\tau)\right), \quad i = 1, 2, \ldots, n.$$

- Exploit system's symmetries to systematically investigate its emergent dynamics.
(FA & Ruan, Nonlinearity 2015)

- Main tools: equivariant bifurcation theory

Systematic classification of dynamical patterns

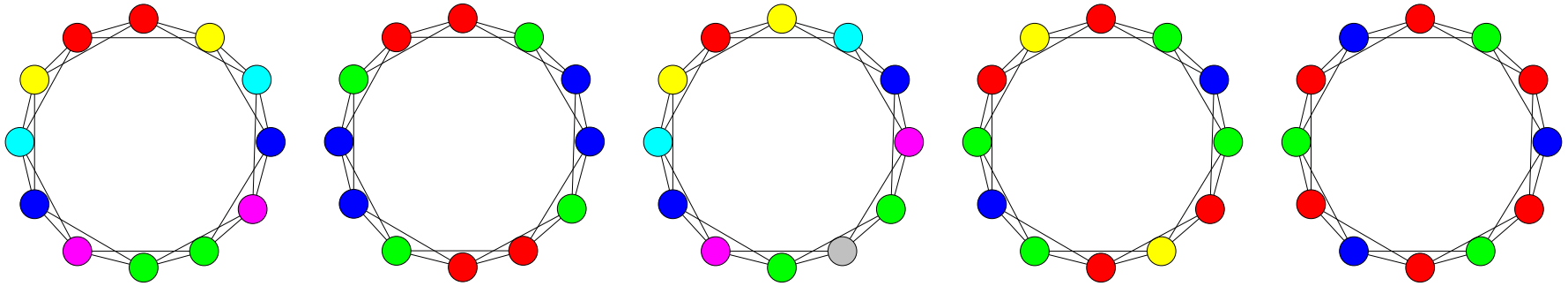
Critical Eigenvalue	Symmetry	Form of Bifurcating Steady-States (for distinct $a, b, c, d, e, f, g \in \mathbb{R}$)	Figure
ξ_0	D_{12}	$(a, a, a, a, a, a, a, a, a, a, a, a)$	
ξ_1 or ξ_5	D_1	$(a, b, c, d, e, f, f, e, d, c, b, a)$	
	$\eta D_1 \eta^{-1}$	$(a, a, b, c, d, e, f, f, e, d, c, b)$	
	$\eta^2 D_1 \eta^{-2}$	$(b, a, a, b, c, d, e, f, f, e, d, c)$	
	$\eta^3 D_1 \eta^{-3}$	$(c, b, a, a, b, c, d, e, f, f, e, d)$	
	$\eta^4 D_1 \eta^{-4}$	$(d, c, b, a, a, b, c, d, e, f, f, e)$	
	$\eta^5 D_1 \eta^{-5}$	$(e, d, c, b, a, a, b, c, d, e, f, f)$	
	$\tilde{D}_1$	$(a, b, c, d, e, f, e, d, c, b, a, g)$	
	$\eta \tilde{D}_1 \eta^{-1}$	$(g, a, b, c, d, e, f, e, d, c, b, a)$	
	$\eta^2 \tilde{D}_1 \eta^{-2}$	$(a, g, a, b, c, d, e, f, e, d, c, b)$	
	$\eta^3 \tilde{D}_1 \eta^{-3}$	$(b, a, g, a, b, c, d, e, f, e, d, c)$	
	$\eta^4 \tilde{D}_1 \eta^{-4}$	$(c, b, a, g, a, b, c, d, e, f, e, d)$	
	$\eta^5 \tilde{D}_1 \eta^{-5}$	$(d, c, b, a, g, a, b, c, d, e, f, e)$	
ξ_2	D_2	$(a, b, c, c, b, a, a, b, c, c, b, a)$	
	$\eta D_2 \eta^{-1}$	$(a, a, b, c, c, b, a, a, b, c, c, b)$	
	$\eta^2 D_2 \eta^{-2}$	$(b, a, a, b, c, c, b, a, a, b, c, c)$	
	$\tilde{D}_2$	$(a, b, c, b, a, d, a, b, c, b, a, d)$	
	$\eta \tilde{D}_2 \eta^{-1}$	$(d, a, b, c, b, a, d, a, b, c, b, a)$	
	$\eta^2 \tilde{D}_2 \eta^{-2}$	$(a, d, a, b, c, b, a, d, a, b, c, b)$	
ξ_3	D_3	$(a, b, b, a, a, b, b, a, a, b, b, a)$	
	$\eta D_3 \eta^{-1}$	$(a, a, b, b, a, a, b, b, a, a, b, b)$	
	$\tilde{D}_3$	$(a, b, a, c, a, b, a, c, a, b, a, c)$	
	$\eta \tilde{D}_3 \eta^{-1}$	$(c, a, b, a, c, a, b, a, c, a, b, a)$	
ξ_4	D_4	$(a, b, a, a, b, a, a, b, a, a, b, a)$	
	$\eta D_4 \eta^{-1}$	$(a, a, b, a, a, b, a, a, b, a, a, b)$	
	$\eta^2 D_4 \eta^{-2}$	$(b, a, a, b, a, a, b, a, a, b, a, a)$	
ξ_6	$\tilde{D}_6$	$(a, b, a, b, a, b, a, b, a, b, a, b)$	

Critical Eigenvalue	Symmetry	Form of Oscillating-States (for some period T)	Figure
ξ_2	$\mathbb{Z}_{12}^{t_2}$	$(x_1(t), x_1(t+\frac{T}{6}), x_1(t+\frac{2T}{6}), \ldots, x_1(t+\frac{5T}{6}),$ $x_1(t), x_1(t+\frac{T}{6}), x_1(t+\frac{2T}{6}), \ldots, x_1(t+\frac{5T}{6}))$	
	$\varsigma \mathbb{Z}_{12}^{t_2} \varsigma^{-1}$	$(x_1(t), x_1(t+\frac{5T}{6}), x_1(t+\frac{4T}{6}) \ldots, x_1(t+\frac{T}{6}),$ $x_1(t), x_1(t+\frac{5T}{6}), x_1(t+\frac{4T}{6}) \ldots, x_1(t+\frac{T}{6}))$	
	D_4^d	$(x_1(t), x_2(t), x_1(t+\frac{T}{2}), x_1(t+\frac{T}{2}), x_2(t), x_1(t),$ $x_1(t), x_2(t), x_1(t+\frac{T}{2}), x_1(t+\frac{T}{2}), x_2(t), x_1(t))$	
	$\eta D_4^d \eta^{-1}$	$(x_1(t), x_1(t), x_2(t), x_1(t+\frac{T}{2}), x_1(t+\frac{T}{2}), x_2(t),$ $x_1(t), x_1(t), x_2(t), x_1(t+\frac{T}{2}), x_1(t+\frac{T}{2}), x_2(t))$	
	$\eta^2 D_4^d \eta^{-2}$	$(x_2(t), x_1(t), x_1(t), x_2(t), x_1(t+\frac{T}{2}), x_1(t+\frac{T}{2}),$ $x_2(t), x_1(t), x_1(t), x_2(t), x_1(t+\frac{T}{2}), x_1(t+\frac{T}{2}))$	
	$D_4^{\hat{d}}$	$(x_1(t), x_2(t), x_1(t), x_1(t+\frac{T}{2}), x_2(t+\frac{T}{2}), x_1(t+\frac{T}{2}),$ $x_1(t), x_2(t), x_1(t), x_1(t+\frac{T}{2}), x_2(t+\frac{T}{2}), x_1(t+\frac{T}{2}))$	
	$\eta D_4^{\hat{d}} \eta^{-1}$	$(x_1(t+\frac{T}{2}), x_1(t), x_2(t), x_1(t), x_1(t+\frac{T}{2}), x_2(t+\frac{T}{2}),$ $x_1(t+\frac{T}{2}), x_1(t), x_2(t), x_1(t), x_1(t+\frac{T}{2}), x_2(t+\frac{T}{2}))$	
	$\eta^2 D_4^{\hat{d}} \eta^{-2}$	$(x_2(t+\frac{T}{2}), x_1(t+\frac{T}{2}), x_1(t), x_2(t), x_1(t), x_1(t+\frac{T}{2}),$ $x_2(t+\frac{T}{2}), x_1(t+\frac{T}{2}), x_1(t), x_2(t), x_1(t), x_1(t+\frac{T}{2}))$	
ξ_3	$\mathbb{Z}_{12}^{t_3}$	$(x_1(t), x_1(t+\frac{T}{4}), x_1(t+\frac{T}{2}), x_1(t+\frac{3T}{4}),$ $x_1(t), x_1(t+\frac{T}{4}), \ldots, x_1(t+\frac{3T}{4}))$	
	$\varsigma \mathbb{Z}_{12}^{t_3} \varsigma^{-1}$	$(x_1(t), x_1(t+\frac{3T}{4}), x_1(t+\frac{T}{2}), x_1(t+\frac{T}{4}),$ $x_1(t), x_1(t+\frac{3T}{4}), \ldots, x_1(t+\frac{T}{4}))$	
	D_6^d	$(x_1(t), x_1(t+\frac{T}{2}), x_1(t+\frac{T}{2}), x_1(t), x_1(t), x_1(t+\frac{T}{2}),$ $x_1(t+\frac{T}{2}), x_1(t), x_1(t), x_1(t+\frac{T}{2}), x_1(t+\frac{T}{2}), x_1(t))$	
	$\eta D_6^d \eta^{-1}$	$(x_1(t), x_1(t), x_1(t+\frac{T}{2}), x_1(t+\frac{T}{2}), x_1(t), x_1(t),$ $x_1(t+\frac{T}{2}), x_1(t+\frac{T}{2}), x_1(t), x_1(t), x_1(t+\frac{T}{2}), x_1(t+\frac{T}{2}))$	
	$\tilde{D}_6^d$	$(x_1(t), x_2(t), x_1(t), x_2(t+\frac{T}{2}), x_1(t), x_2(t),$ $x_1(t), x_2(t+\frac{T}{2}), x_1(t), x_2(t), x_1(t), x_2(t+\frac{T}{2}))$	
	$\eta \tilde{D}_6^d \eta^{-1}$	$(x_2(t+\frac{T}{2}), x_1(t), x_2(t), x_1(t), x_2(t+\frac{T}{2}),$ $x_1(t), x_2(t), x_1(t), x_2(t+\frac{T}{2}), x_1(t), x_2(t), x_1(t))$	

(FA & Ruan, Nonlinearity 2015)

- Some example patterns for neural network type models:

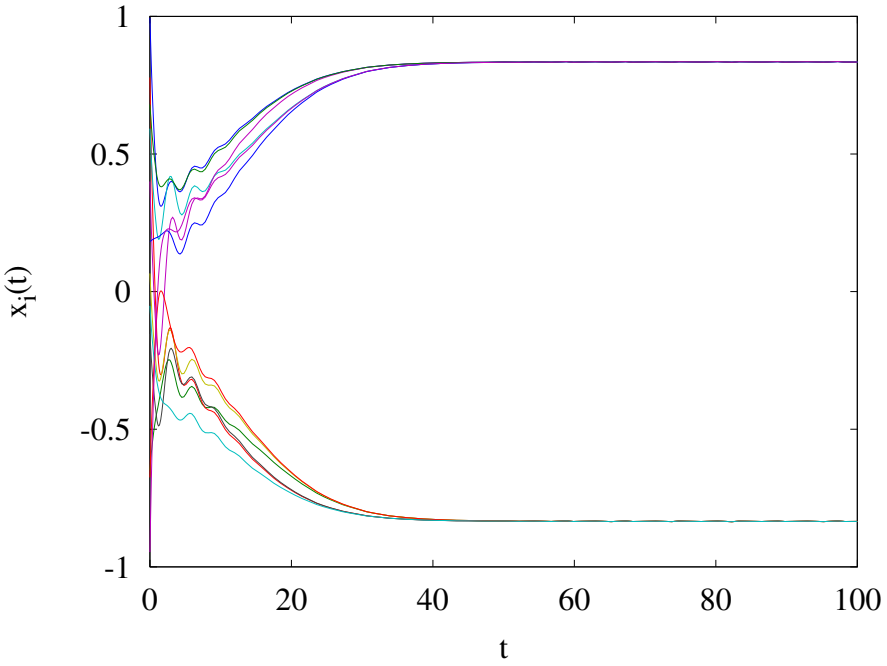
$$\dot{x}_i(t) = -x_i(t) + g\left(\sum_{j=1}^{n} a_{ij} x_j(t-\tau)\right), \quad i = 1, 2, \ldots, n.$$



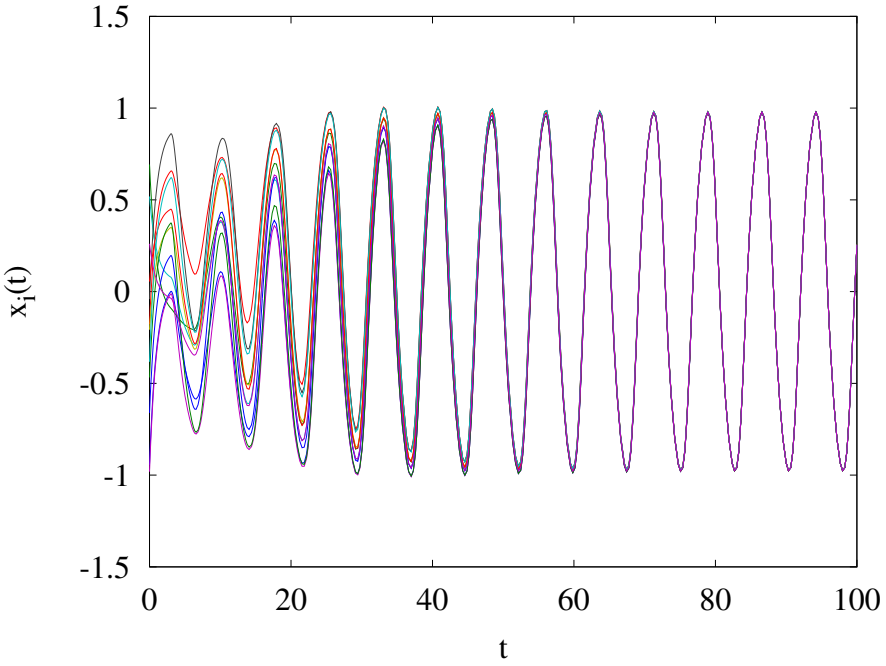
(FA & Ruan, Nonlinearity 2015)

Examples

Spatial vs. temporal complexity



$\tau = 1$, two-cluster steady-state



$\tau = 3$, synchronized periodicity