# Restrictions and unfolding of local bifurcations in delay-differential equations modelling biological phenomena.

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# Delay Equations as Biological Models

- Motor control with delay: Bélair, Beuter, Campbell.

$$\dot{x} = a_1 f_1(x(t-\tau_1)) + a_2 f_2(x(t-\tau_2)), \quad x(\cdot) \in \mathbb{R},\ \tau_1, \tau_2 > 0.$$

- Pupil light reflex: Longtin and Milton.

$$\ddot{x} + \alpha\dot{x} + \beta x = f(x(t-\tau)), \quad x(\cdot) \in \mathbb{R},\ \tau > 0.$$

- Drug Delivery model:

$$\begin{aligned} [\dot{S}] &= \gamma\Phi([P](t-\tau))([S]^* - [S]) - \kappa[S] \\ [\dot{P}] &= \kappa[S] - \gamma\Psi([P](t-\tau))([P] - [P]^*). \end{aligned}$$

- Neural networks: $\mathbf{D}_3$-symmetric system

$$\dot{x}_j = -u_j(t) + \alpha u_j(t-\tau_s) + \beta\left[u_{j-1}(t-\tau_n) + u_{j+1}(t-\tau_n)\right],\ j = 1, 2, 3$$

# Linear theory of DDEs

1. Let $C_n = C([-\tau, 0], \mathbb{R}^n)$, $x_t : C_n \to \mathbb{R}^n$; $x_t(\theta) = x(t+\theta)$, $L : C_n \times \mathbb{R}^p \to \mathbb{R}^n$, and $f : C_n \times \mathbb{R}^p \to \mathbb{R}^n$ ($C^\infty$)

$$\dot{x} = L(\alpha)x_t + f(x_t, \alpha)$$

2. Linear flow: $\dot{x} = L(\alpha)x_t$
3. Linear operator $L$ is bounded

$$L(\alpha)\phi = \int_{-\tau}^{0} d\eta(\theta, \alpha)\phi(\theta),$$

where $\eta$ is a $n \times n$ matrix-valued function of bounded variation.

4. $L_0 = L(0)$ and $A_0$: infinitesimal operator of the semiflow. We have $\lambda \in \sigma(A_0)$ if

$$\det \Delta(\lambda) = 0, \quad \Delta(\lambda) = \lambda I_n - \int_{-\tau}^{0} d\eta(\theta)\phi(\theta).$$

# Double Hopf Bifurcation

- Critical eigenvalues: $\Lambda = \{\lambda \in \mathbb{C} \mid \det \Delta(\lambda) = 0$ and $\lambda = i\omega\}$.
- A nonresonant double Hopf bifurcation occurs if

$$\Lambda = \{\pm i\omega_1, \pm i\omega_2\} \qquad \text{with } \omega_1/\omega_2 \notin \mathbb{Q}.$$

- The normal form of the (nonresonant) double Hopf bifurcation is

$$\begin{aligned} \dot{z}_1 &= p_1(|z_1|^2, |z_2|^2)z_1 \\ \dot{z}_2 &= p_2(|z_1|^2, |z_2|^2)z_2 \end{aligned}$$

- The dynamics is determined by the third order truncation

$$\begin{aligned} \dot{z}_1 &= (i\omega_1 + c_{11}|z_1|^2 + c_{12}|z_2|^2)z_1 \\ \dot{z}_2 &= (i\omega_2 + c_{21}|z_1|^2 + c_{22}|z_2|^2)z_2 \end{aligned}$$

if Re $(c_{ij}) \neq 0$, Re $(c_{11})$Re $(c_{22})$ − Re $(c_{12})$Re $(c_{21}) \neq 0$.

# Invariant and Centre Manifold Theorem

The spectrum of the infinitesimal operator $A_0$ induces a splitting

$$C_n = E^s \oplus E^c \oplus E^u$$

where $E^s, E^u$ are the invariant stable and unstable subspaces and $E^c$ is the centre subspace of dimension $m$ spanned by the generalized eigenvectors of $\Lambda$.
There exists a $m$-dimensional local centre manifold $M_f$ near $(0,0)$ defined by

$$M_f = \{\phi \in C_n \mid \phi = \Phi x + h(x,f),\, x \in \mathbb{R}^m \text{ in a nbhd of } 0\}$$

where $\Phi(\theta) = (\phi_1(\theta), \ldots, \phi_m(\theta))$ is a basis of $E^c$ and $h(x,f) \in E^s \oplus E^u$ is $C^N$.

# Reduced equation on the centre manifold

Let $\Psi(s) = \text{col}(\psi_1(s), \ldots, \psi_m(s))$ be a basis of the dual space $(E^c)^*$ via the bilinear form

$$(\psi, \phi) = \psi(0)\psi(0) - \int_{-\tau}^{0} \int_{0}^{\theta} \alpha(\xi - \theta)[d\eta(\theta)]\phi(\xi)d\xi.$$

Then the flow on the centre manifold is given by $z_t = \Phi x(t) + h(x(t), f)$ where $x(t)$ is solution to the ordinary differential equation

$$\dot{x} = B_0 x + \Psi(0) f(\Phi x + h(x, f))$$

with $A_0 \Phi = \Phi B_0$, $B_0 = \text{diag}(\lambda_1, \ldots, \lambda_m)$ where $\lambda_i \in \Lambda$ for all $i = 1, \ldots, m$.

# Realisation Theorems (Faria and Magalhaes)

- DDE: set of delay-differential equations.
- LDDE: set of linear DDEs.
- ODE: set of ordinary differential equations.
- LODE: set of linear ODEs.
- FJODE: set of finite jets of ODEs.
- $\mathcal{P}_{CM}$: Map to center manifold reduced equation.

1. Thm 1: $\mathcal{P}_{CM} : DDE \to ODE$ is surjective ($\equiv$realisation).
2. Thm 2: $\mathcal{P}_{CM} : DDE \to FJODE$ realisation can be achieved with $m - q + 1$ nonlinear delays where $m = \dim E^c$ and $q =$ rank $\Phi(0)$.
3. Thm 3: $\mathcal{P}_{CM} : LDDE \to LODE$ is surjective iff $n \geq max\{\#$Jordan blocks of $\lambda \mid \lambda \in \Lambda\}$.

# Linear and nonlinear unfoldings

- Different approach: compute linear and nonlinear unfoldings at bifurcations.
- Some simple cases are already known when realisation results do not apply.

Generically, there are no restrictions on the dynamics, if

1. $\dot{z} = \nu z(t-\tau_0) + L_0 z_t + A(z(t-\tau_0))^3$
   with $A, \nu \in \mathbb{R}$ at a Hopf bifurcation point. (Faria and Magalhaes)
2. $\dot{z} = \nu_1 z(t) + \nu_2 z(t-\tau_0) + L_0 z_t + A(z(t-\tau_0))^2 + Bz(t)z(t-\tau_0)$
   with $\nu_1, \nu_2, A, B, C \in \mathbb{R}$ at a Bogdano-Takens point. (F-M)
3. $\dot{z} = \nu_1 z(t) + \nu_2 z(t-\tau_0) + L_0 z_t + Az(t)^3 + Bz(t-\tau_0)^3$
   with $\nu_1, \nu_2, A, B \in \mathbb{R}$ at a B-T point with $\mathbf{z}_2$-symmetry. (Redmond, LeBlanc, Longtin).

*Note that the linear and nonlinear unfoldings above are not unique.*

# Nonlinear restrictions: first case

Motor control task model (Bélair, Beuter *et al.*)

$$\dot{x} = a_1 f_1(x(t-\tau_1)) + a_2 f_2(x(t-\tau_2)) \tag{1}$$

with $f_1, f_2$ odd functions (i.e. $\mathbf{Z}_2$-symmetric).

• Result: At a double Hopf bifurcation point of equation (1) there are nonlinear restrictions on the possible dynamics.

• Centre manifold reduction yields

$$\begin{aligned} \dot{r}_1 &= (\text{Re}\,(c_{11}) r_1^2 + \text{Re}\,(c_{12}) r_2^2) r_1 \\ \dot{r}_2 &= (\text{Re}\,(c_{21}) r_1^2 + \text{Re}\,(c_{22}) r_2^2) r_2 \end{aligned}$$

where $\text{Re}\,(c_{12}) = 2\text{Re}\,(c_{11})$ and $\text{Re}\,(c_{21}) = 2\text{Re}\,(c_{22})$.
Restrictions: Out of the $12$ cases of unfolding, $6$ are prohibited.

# Double Hopf bifurcation: scalar case

- Consider the scalar DDEs

$$\dot{z} = L_0 z_t + f(z(t-\tau_1), z(t-\tau_2))$$

and

$$\dot{z} = L_0 z_t + f(z(t-\tau)).$$

**Theorem 1 (B. and Bélair)** *Generically, at a nonresonant double Hopf bifurcation, there are no restrictions on the dynamics of*

- $\dot{z} = \nu_1 z(t-\tau_1) + \nu_2 z(t-\tau_2) + L_0 z_t + f(z(t-\tau_1), z(t-\tau_2))$ *for $f$ **Z**$_2$-symmetric and for general $f$, however*
- $\dot{z} = \nu_1 z(t-\tau_1) + \nu_2 z(t-\tau_2) + L_0 z_t + f(z(t-\tau))$ *always has nonlinear restrictions on the possible flows near bifurcation. But no linear restrictions.*

- Therefore, the restrictions on the dynamics in the motor control task model come from the structure of the model.

# Nonlinear restrictions: second case

Harmonic oscillator with delayed feedback of Longtin and Milton, Campbell et al.

$$\ddot{x} + \alpha\dot{x} + \beta x = f(x(t-\tau)).$$

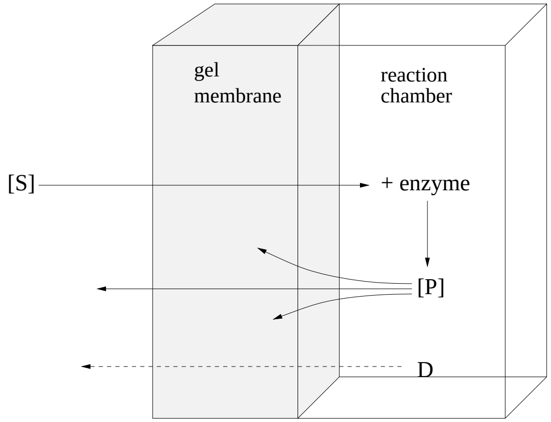
**Theorem 2 (B. and Bélair)** *Suppose that the $n^{th}$-order delay-differential equation ($n \geq 2$)*

$$u^{(n)} + \beta u^{(n-1)} + \cdots + \beta_n u = f(u(t-\tau))$$

*has a nonresonant double Hopf bifurcation. Then, generically, there are always nonlinear restrictions on the possible flows near bifurcation. The linear unfolding yields no restrictions.*

*proof*: This case can be reduced to the first-order scalar case with one nonlinear delay: $\dot{z} = L_0 z_t + f(z(t-\tau))$

# Drug Delivery System: Siegel et al.




- $S$: substrate, $P$: product, $D$: drug.
- $[S^*]$ and $[P^*]$: fixed external concentrations.
- $[P]$ induces swelling and deswelling of the membrane.
- Permeability of the membrane to $S$ and $P$: $M([P])$, $N([P])$.
- Delay induced by the transport time from chamber inside membrane.

# Drug Delivery System: Bélair and B.

Siegel and Pitt equations (Hopf bifurcation):

$$\begin{aligned} [\dot{S}] &= \gamma K(t)([S]^* - [S]) - \kappa[S] \\ [\dot{P}] &= \kappa[S] - \gamma q[P] \end{aligned}$$

where $\gamma =$membrane area/volume chamber, $q$ membrane permeability to $[P]$ and $K(t)$ membrane permeability to $[S]$

$$\dot{K} = \alpha(K_\infty - K)$$

Modified Siegel and Pitt equations (Hopf and double Hopf):

$$\begin{aligned} [\dot{S}] &= \gamma M([P](t-\tau))([S]^* - [S]) - \kappa[S] \\ [\dot{P}] &= \kappa[S] - \gamma N([P](t-\tau))([P] - [P]^*). \end{aligned}$$

# Hopf and double Hopf points

Equilibrium solution $([S]_0, [P]_0)$

$$\begin{aligned} \dot{u} &= -\alpha u - \beta v(t-\tau) + f(u(t), v(t-\tau)) \\ \dot{v} &= u - N([P]_0)v - bv(t-\tau) + g(v(t), v(t-\tau)). \end{aligned}$$

Characteristic equation (studied by Cooke and Grossman (1982))

$$\lambda^2 - a\lambda + b\lambda e^{-\lambda\tau} + c + de^{-\lambda\tau} = 0$$

where $b = N([P]_0)([P]_0 - [P]^*)$, $d = \alpha b + \beta$.

**Theorem 3** *Suppose that $c + d > 0$ and $b \in (-a, -\sqrt{a^2 - 2c})$. There exists $\beta_{inf} < \beta_- < \beta_+ < \beta_{sup}$ such that if*

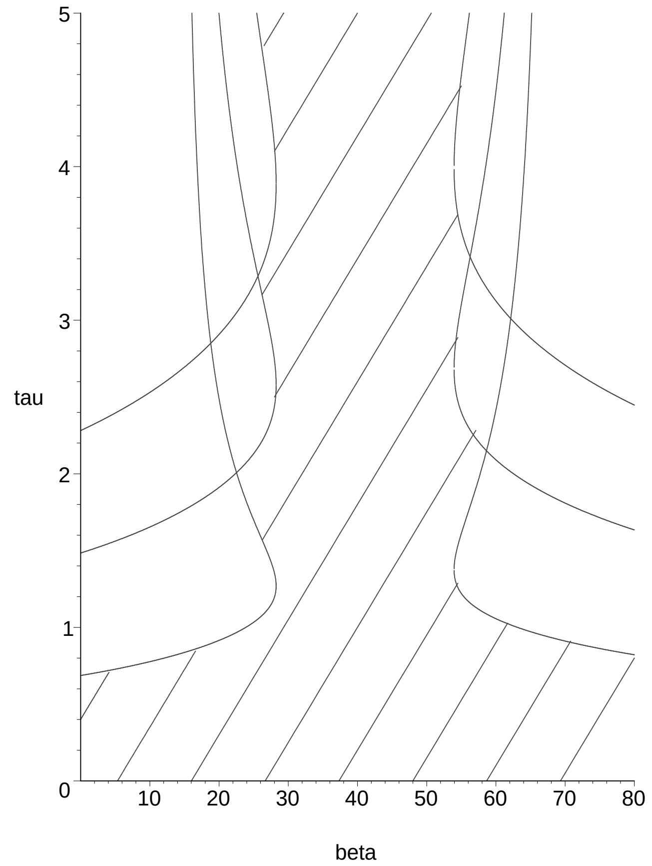
$$\beta \in (\beta_{inf}, \beta_-) \cup (\beta_+, \beta_{sup})$$

*then there are multiple changes of stability of the equilibrium as the delay is increased from $\tau = 0$.*

# Hopf and double Hopf points

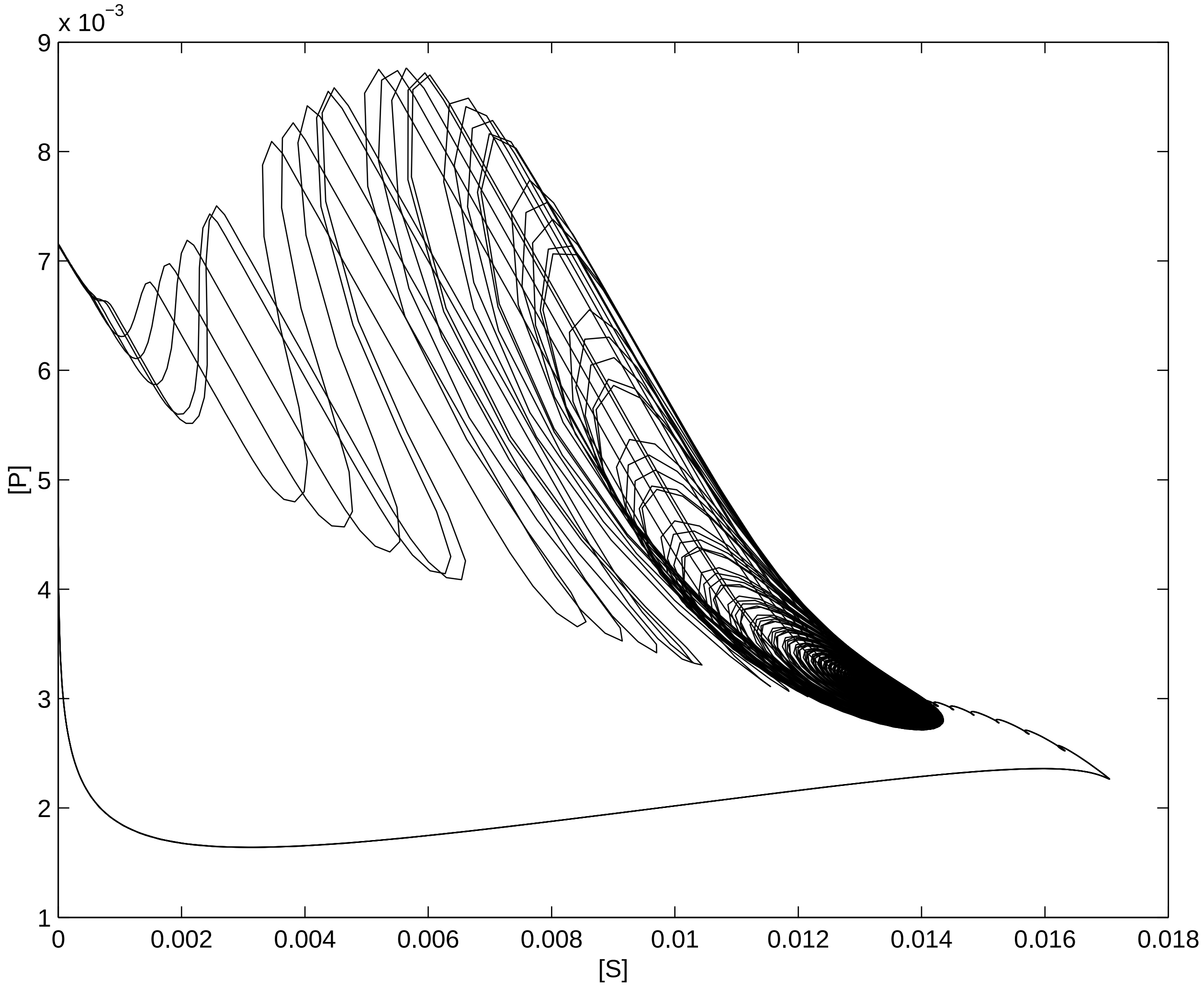
Stability diagram for

$$a \approx 10.59,\ b \approx -10.27,\ c \approx 26.37,\ \alpha \approx 4.00,\ \beta \approx 24.62$$



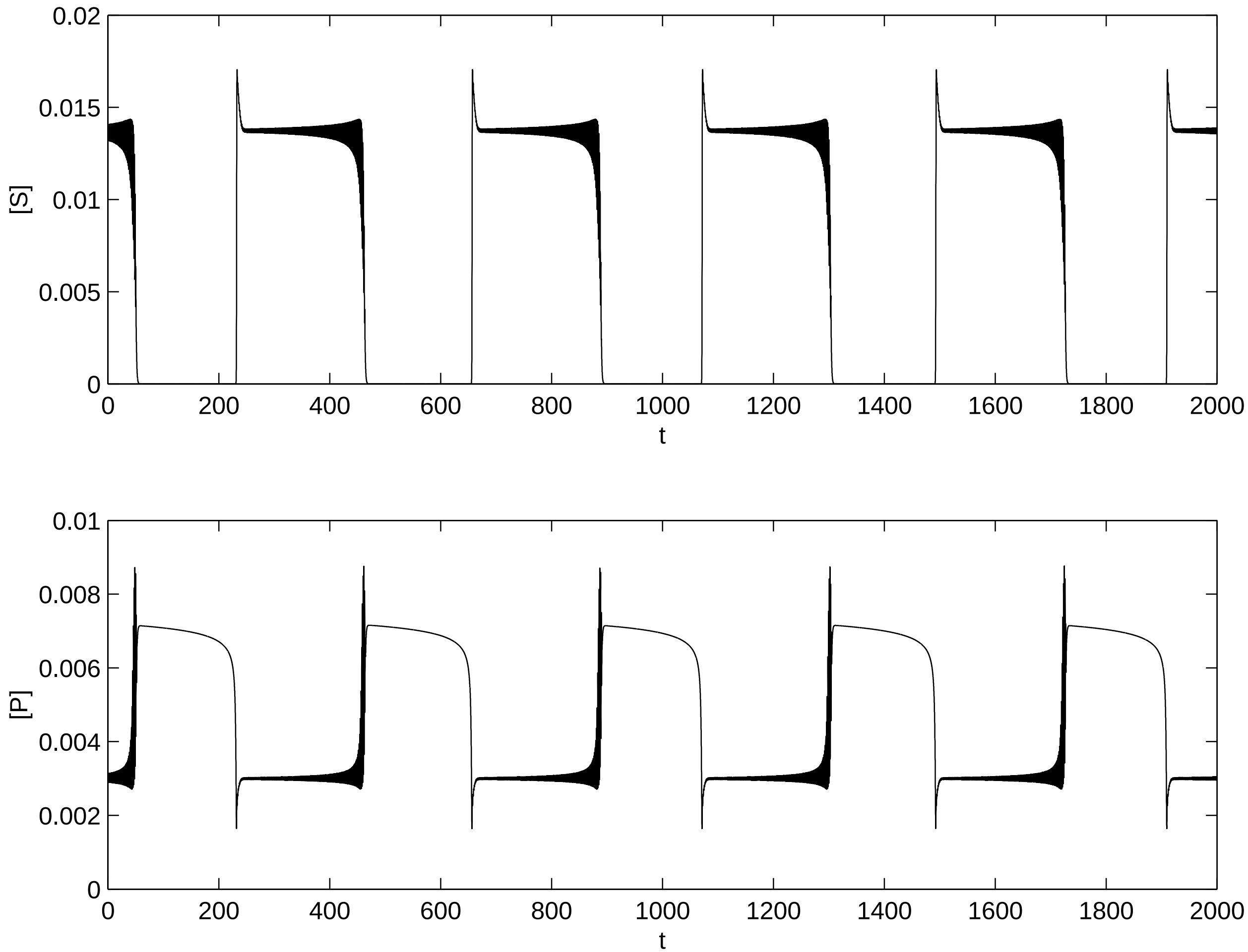
# Numerical Simulations

Numerical simulations using realistic permeability functions near the Hopf bifurcation curve:



# Gibbs' like behaviour

Periodic solutions with "Gibbs like" behaviour due to special form of the permeability functions (see also Mallet-Paret and Nussbaum).



# Linear unfolding of the double Hopf point

- Nonresonant double Hopf bifurcation at $([S]_0, [P]_0)$: $\pm i\omega_1$, $\pm i\omega_2$.

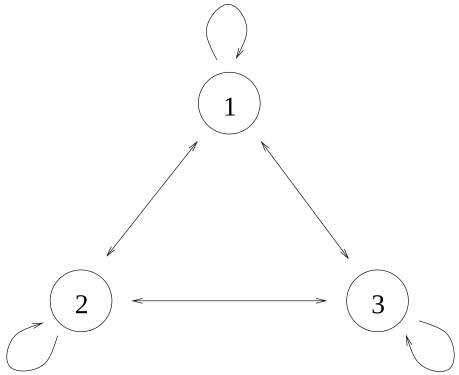
- The unfolding restricted to the model is:

$$\begin{aligned}\dot{u} &= -(\Phi([P]_0) + 1)u + \Phi'([P_0])([S]^* - [S]_0)v(t-\tau) \\ \dot{v} &= (1+\epsilon_1)u + (\epsilon_2 - \Psi([P_0]))v + (\epsilon_3 - b)v(t-\tau),\end{aligned}$$

where generically, eigenvalues near the bifurcation point are given by

$$\epsilon_2 + \omega_1(h(\epsilon_1, \epsilon_2, \epsilon_3)), \quad \epsilon_3 + \omega_2(h(\epsilon_1, \epsilon_2, \epsilon_3)),\ h \text{ smooth.}$$

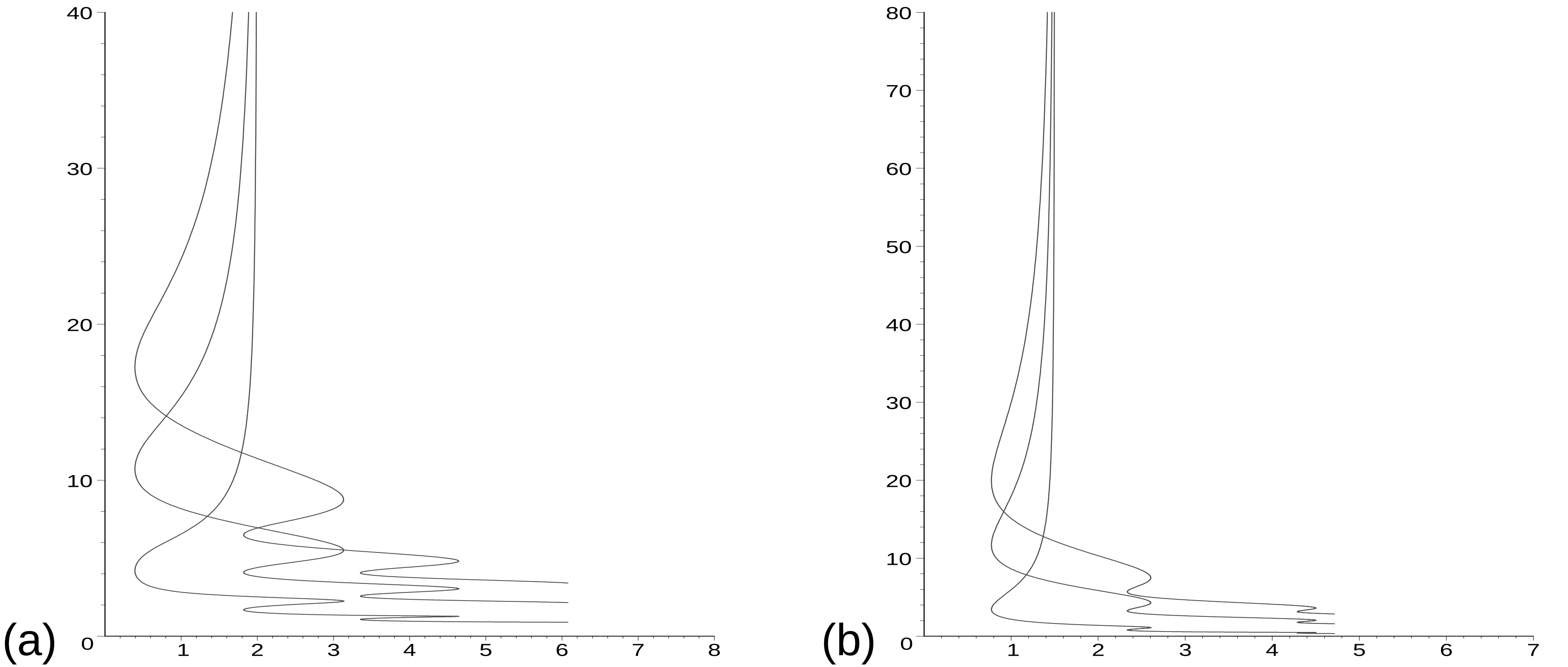
# Symmetrically Coupled DDEs




$D_3$ - symmetric system

$$\begin{aligned}
\dot{u}_1(t) &= -u_1(t) + \alpha u_1(t-\tau_s) + \beta\left[u_3(t-\tau_n) + u_2(t-\tau_n)\right], \\
\dot{u}_2(t) &= -u_2(t) + \alpha u_2(t-\tau_s) + \beta\left[u_1(t-\tau_n) + u_3(t-\tau_n)\right], \\
\dot{u}_3(t) &= -u_3(t) + \alpha u_3(t-\tau_s) + \beta\left[u_2(t-\tau_n) + u_1(t-\tau_n)\right].
\end{aligned}$$

# Double Hopf bifurcation




This equation has double Hopf bifurcation points without symmetry and with $\mathbf{D}_3$ symmetry from the standard representation.

# Linear unfolding of the double Hopf point

$$\begin{aligned}
\dot{u}_1(t) &= (-1+\epsilon_1)u_1(t) + (\alpha^* + \epsilon_2)u_1(t-\tau_s^*) \\
&+ (\beta^* + \epsilon_3)(u_3(t-\tau_n^*) + u_2(t-\tau_n^*)) + \epsilon_4(u_3(t-\tau_3) + u_2(t-\tau_3))
\end{aligned}$$

$$\begin{aligned}
\dot{u}_2(t) &= (-1+\epsilon_1)u_2(t) + (\alpha^* + \epsilon_2)u_2(t-\tau_s^*) \\
&+ (\beta^* + \epsilon_3)(u_1(t-\tau_n^*) + u_3(t-\tau_n^*)) + \epsilon_4(u_1(t-\tau_3) + u_3(t-\tau_3))
\end{aligned}$$

$$\begin{aligned}
\dot{u}_3(t) &= (-1+\epsilon_1)u_3(t) + (\alpha^* + \epsilon_2)u_3(t-\tau_s^*) \\
&+ (\beta^* + \epsilon_3)(u_2(t-\tau_n^*) + u_1(t-\tau_n^*)) + \epsilon_4(u_2(t-\tau_3) + u_1(t-\tau_3)).
\end{aligned}$$

Set $\epsilon_4 = 0$ to respect the structure of the model. As before, generically the eigenvalues near the bifurcation point are

$$\epsilon_2 + \omega_1(h(\epsilon_1, \epsilon_2, \epsilon_3)), \quad \epsilon_3 + \omega_2(h(\epsilon_1, \epsilon_2, \epsilon_3)), \ h \text{ smooth.}$$

**Open question:** Is it always the case that the real part of the eigenvalues at a bifurcation point can be unfolded within the model?

# Linear unfolding theory

Consider the parametrized family of DDEs:

$$\dot{z} = L(\alpha)z_t + f(z_t, \alpha)$$

such that $L(0) = L_0$ has $\Lambda \neq \emptyset$.
The parametrized centre manifold reduced equation is

$$\dot{x} = B(\alpha)x + G(x)$$

where $B(0) = B_0 = \text{diag}(\lambda_1, \ldots, \lambda_m)$.

**Question 1** *Given a versal unfolding $B(\alpha)$ of $B_0$, can we construct an unfolding $L(\alpha)$ of $L_0$ which maps to $B(\alpha)$ via the centre manifold reduction?*

**Answer 1 (B. and LeBlanc)** *Yes and we call such an unfolding $L(\alpha)$ a* $\Lambda$-versal unfolding *of $L_0$.*

# Linear Unfolding Theorem(B. and LeBlanc)

Let $m = \dim E^c$, $q = \text{rank}\,\Phi(0)$, $\alpha_k \in \mathbb{C}$ and $z \in C([-\tau, 0], \mathbb{C}^n)$. We can construct $n \times n$ matrices $A_j^k$ such that if

$$L_k(z) = \sum_{j=0}^{m-q} A_j^k z(\tau_j)$$

and

$$L(\alpha) = L_0 + \sum_{k=1}^{m} \alpha_k L_k,$$

then

$L(\alpha)$ is a $\Lambda$-miniversal unfolding of $L_0$.

# Extensions

- A straightforward decomplexification procedure yields the real $\Lambda$-versal unfolding of $L_0$.
- Let $\Gamma$ be a compact Lie group and $L_0$ be $\Gamma$-equivariant, then $L(\alpha)$ can be chosen to be $\Gamma$-equivariant.

  Key idea: Projection to spaces of $\Gamma$-equivariant matrices.

  $$\pi_n^\Gamma(A) = \int_\Gamma \gamma A \gamma^{-1} d\gamma, \qquad \pi_m^\Gamma(M) = \int_\Gamma G(\gamma) M G(\gamma^{-1}) d\gamma,$$

  where $G$ is the representation on $E^c$. (B and LeBlanc)

  Note that $\Lambda$-versal unfoldings project to $\Gamma$-equivariant $\Lambda$-versal unfoldings but miniversality is not necessarily preserved.