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Numerical bifurcation analysis of infinite-delay equations in biology

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WHY?
motivation and background

Example from ecology

an age-structured population

Renewal equation for population birth rate

$$b(t) = \int_{a_{\text{repr}}}^{a_{\max}} \overbrace{\beta(a)}^{\text{fertility}} \, \overbrace{\mathcal{F}(a)\, b(t-a)}^{\text{ind of age } a} \, da$$

often coupled with a delay-differential equation for the environmental variable (substrate, prey,...)

$$\frac{dS}{dt}(t) = \underbrace{f(S(t))}_{\text{consumer-free}} - \int_{0}^{a_{\max}} \overbrace{\gamma(a)}^{\text{consumption}} \, \overbrace{\mathcal{F}(a)\, b(t-a)}^{\text{ind of age } a} \, da$$

Why…

…infinite delay?

- to model the effect of the past on the present
  (reproduction of individuals, retarded signals or reactions, …)
- mathematically, probability densities have infinite support
  (exponential, gaussian,…)
- biologically, impossible a priori bounds
  (history of local habitats, beginning of an epidemic,…)

Why…

…numerical bifurcation analysis?

- interest in long-term behaviour
  (persistence/extinction, equilibria/periodic, chaos,…)
- influence of model parameters
- complicated models, very complicated (impossible?) analytical results
- increasing applications to real biological systems
  (size-structured populations, stem cells models,…)

Our approach: pseudospectral discretization

INPUT:
nonlinear delay system

↓

APPROXIMATION WITH ODEs
+
SOFTWARE FOR ODEs

↓

OUTPUT: bifurcation analysis

[Breda, Diekmann, Gyllenberg, S., Vermiglio, *SIAM J. Appl. Dyn. Syst.*, 2016]

WHAT?
delay equations

Delay equation

a rule for extending a function given its past

Let $\tau > 0$ be the maximal delay and $\mathcal{I}$ the delay interval:

- if $\tau < \infty$, let $\mathcal{I} = [-\tau, 0]$
- if $\tau = \infty$, let $\mathcal{I} = (-\infty, 0]$

Given a function y, we define the history function $y_t : \mathcal{I} \to \mathbb{R}^d$

$$y_t(\theta) = y(t + \theta), \quad \theta \in \mathcal{I}$$

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$y_t \in Y$ space of functions $\quad \to$ infinite dimension!

Weighted state-spaces for $\tau = \infty$

- $\rho > 0$ scaling parameter
- $w(\theta) = e^{\rho\theta}$ weight function on $\mathcal{I} = (-\infty, 0]$
- $\hat{\psi}(\theta) := w(\theta)\psi(\theta)$ for any $\psi \colon \mathcal{I} \to \mathbb{R}^d$
- weighted spaces

$$L^1_\rho(\mathcal{I}, \mathbb{R}^d) := \{\varphi \colon \mathcal{I} \to \mathbb{R}^d \text{ s.t. } \int_{\mathcal{I}} |\hat{\varphi}(\theta)| d\theta < \infty\}$$

$$C_{0,\rho}(\mathcal{I}, \mathbb{R}^d) := \{\psi \colon \mathcal{I} \to \mathbb{R}^d \text{ s.t. } \sup_{\theta \in \mathcal{I}} |\hat{\psi}(\theta)| < \infty, \lim_{\theta \to -\infty} \hat{\psi}(\theta) = 0\}$$

- note: constant functions belong to L^1_ρ and $C_{0,\rho}$
- (if $\tau < \infty$, we take $\rho = 0$)

We consider

renewal:	$x(t) = F(x_t)$	$F \colon X \to \mathbb{R}^d$ $X = L^1_\rho(\mathcal{I}, \mathbb{R}^d)$
differential:	$\dot{y}(t) = G(y_t)$	$G \colon Y \to \mathbb{R}^d$ $Y = C_{0,\rho}(\mathcal{I}, \mathbb{R}^d)$
coupled systems:	$\begin{cases} x(t) = F(x_t, y_t) \\ \dot{y}(t) = G(x_t, y_t) \end{cases}$	$F, G \colon X \times Y \to \mathbb{R}^d$

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For notational convenience:

- $d = 1$
- delay differential equations

From IVP to ACP

Initial value problem for $y(t)$

$$\begin{cases} \dot{y}(t) = G(y_t) & t \geq 0 \\ y(\theta) = \psi(\theta) & \theta \in \mathcal{I} \end{cases}$$

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$$\Updownarrow$$

Abstract Cauchy problem for $v(t) := y_t \in Y$

$$\begin{cases} \dot{v}(t) = \mathcal{A}(v(t)) & t \geq 0 \\ v(0) = \psi \end{cases}$$

where $\mathcal{A}$ is the infinitesimal generator of the family of solution operators:

$$\mathcal{A}(\psi) = \psi', \quad \psi \in D(\mathcal{A})$$
$$D(\mathcal{A}) = \{\psi \in Y \text{ s.t. } \psi' \in Y \text{ and } \psi'(0) = G(\psi)\}$$

Stability of equilibria

Principle of linearized stability

G continuously Fréchet differentiable, $\bar{y}$ equilibrium. Then the stability of $\bar{y}$ is determined by the linearized system:

- if all the roots of the characteristic equation have negative real part, $\bar{y}$ is exponentially stable
- if there exists a root with positive real part, $\bar{y}$ is unstable.

Properties of a linear $\mathcal{A}$

- $\mathcal{A}$ is not compact, ($\sigma(\mathcal{A})$ has not only eigenvalues)
- there exists $\overline{\rho} > 0$ such that $\{\Re(\lambda) > -\overline{\rho}\}$ contains only eigenvalues, and they are roots of the characteristic equation
- freedom of choice $0 < \rho < \overline{\rho}$

[Diekmann, Gyllenberg, *SIAM J. Differential Equations*, 2012]

HOW?

pseudospectral discretization

Discretization

Mesh of $M+1$ nodes in $\mathcal{I}$

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function in Y $\approx$ polynomial of degree M

$$\psi(\theta) \approx p_M(\theta) = \sum_{j=0}^{M} \ell_j(\theta)\psi(\theta_j)$$

with $\ell_j(\theta)$ Lagrange polynomials: $\ell_j(\theta) = \prod_{k \neq j} \dfrac{\theta - \theta_k}{\theta_j - \theta_k}$

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$$\hat{\psi}(\theta) \approx \hat{p}_M(\theta) = e^{\rho\theta} \sum_{j=0}^{M} \ell_j(\theta) \frac{\hat{\psi}(\theta_j)}{e^{\rho\theta_j}}$$

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Pseudospectral collocation

$$v_0(t) \approx v(t)(0),$$
$$\hat{v}_j(t) \approx e^{\rho\theta_j} v(t)(\theta_j),\ j = 1, \ldots, M$$
$$\overrightarrow{V} = (\hat{v}_1, \ldots, \hat{v}_M)^T \in \mathbb{R}^{dM}$$

so that

$$v(t) \approx p_M(v_0, \overrightarrow{V}) = \ell_0(\theta) v_0(t) + \sum_{j=1}^{M} \ell_j(\theta) \frac{\hat{v}_j(t)}{e^{\rho\theta_j}}$$

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"The polynomial p_M satisfies exactly the abstract equation on the nodes"

Abstract equation in Y

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$$v(t) \in D(\mathcal{A}) = \{\psi'(0) = G(\psi)\}$$

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Abstract equation in Y		ODE in $\mathbb{R}^{d(M+1)}$
$\dot{v}(t) = \mathcal{A}(v(t))$	$\Rightarrow$	$\dot{\overrightarrow{V}} = \hat{D}_M \overrightarrow{V} + \hat{d}_M v_0 - \rho \overrightarrow{V}$
$v(t) \in D(\mathcal{A}) = \{\psi'(0) = G(\psi)\}$		$\dot{v}_0 = G(p_M(v_0, \overrightarrow{V}))$

A closer look at the ODE system

$$\boxed{\begin{aligned} \dot{\overrightarrow{V}} &= \hat{D}_M \overrightarrow{V} + \hat{d}_M v_0 - \rho \overrightarrow{V} \\ \dot{v}_0 &= G(p_M(v_0, \overrightarrow{V})) \end{aligned}}$$

The matrices $\hat{d}_M \in \mathbb{R}^{dM}$, $\hat{D}_M \in \mathbb{R}^{dM \times dM}$ are

- independent of the specific delay equation
- explicitly available from the nodes: $\hat{d}_{ij} = e^{\rho(\theta_i - \theta_j)} \ell_j'(\theta_i),\ i, j = 0, \dots, M$

$G \colon Y \to \mathbb{R}^d$

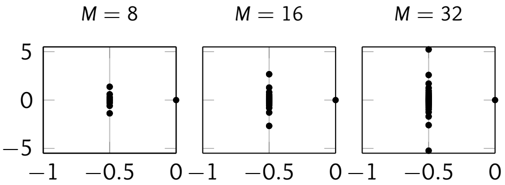
- appears only in the equation for v_0
- applied to the interpolating polynomial, no special assumptions
- in the case of RE, we apply the implicit function theorem:
  $u_0 = F(p_M(u_0, \overrightarrow{U})) \Rightarrow u_0 = \tilde{F}_M(\overrightarrow{U})$

Approximation of equilibria and their stability

- one-to-one correspondence of equilibria
- $\tau < \infty$ and Chebyshev extremal nodes: eigenvalues are approximated with spectral accuracy: error bound $\varepsilon(M) = O\left(M^{-k}\right)$, for any $k \in \mathbb{N}$

  Breda, Maset, Vermiglio, *SIAM J. Sci. Comput.*, 2005
- $\tau = \infty$: spectral accuracy is conjectured. With Laguerre nodes (orthogonal w.r.t. $e^{\rho\theta}$), the spurious eigenvalues align along $\Re\lambda = -\rho$

extrema
plus zero
$\rho = 0.5$



some results

…but first, a recap

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OUTPUT: bifurcation analysis

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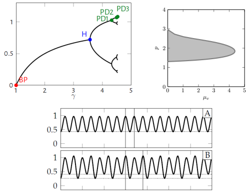
"G"

$$\begin{cases} \dot{\vec{V}} = \hat{D}_M \vec{V} + \hat{d}_M v_0 - \rho \vec{V} \\ \dot{v}_0 = G(p_M(v_0, \vec{V})) \end{cases}$$



A physiologically structured model

model definition

$$\begin{cases} b(t) &= \int_0^\infty \beta(a, S_t)\mathcal{F}(a)b(t-a)da \\ \dot{S}(t) &= rS(t)\left(1 - \frac{S(t)}{K}\right) - \int_0^\infty \gamma(a, S_t)\mathcal{F}(a)b(t-a)da \end{cases}$$

$$\mathcal{F}(a) = e^{-\mu a}, \quad \beta(a, S_t) = \alpha\gamma(a, S_t), \quad \gamma(a, S_t) = \frac{S(t)}{1+S(t)}\ell(a; S_t)^2$$

where α, μ, r, K are positive parameters and $\ell(a; S_t)$ is the length of an individual that has age a at time t, defined by

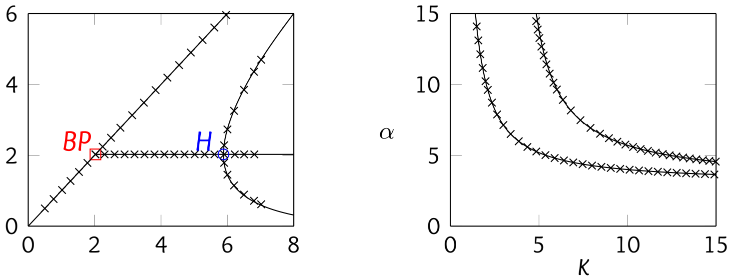
$$\ell(a; S_t) := \int_0^a \frac{S(t-\sigma)}{1+S(t-\sigma)}e^{-\sigma}d\sigma.$$

A physiologically structured model

analysis with Matcont for Matlab, software for ODEs

Output of the pseudospectral discretization for $M = 20$, $\rho = \frac{\mu}{2}$
and reference values obtained from equivalent ODE formulation (crosses)

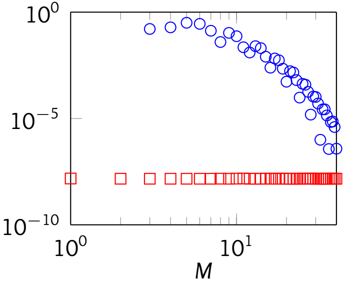
Bifurcation diagram w.r.t. K Stability regions in (K, α)



A physiologically structured model

numerical error

Error in detection of BP and H, increasing M.
Notice spectral accuracy



Gyllenberg, S., Vermiglio, *submitted*, 2017

Conclusions

- potentially "automatic" discretization for general DEs
- exploits pre-existing software for ODEs

…and open problems

- convergence of eigenvalues $\tau = \infty$ (requires suitable bounds of interpolation error)
- approximation of periodic solutions (also for $\tau < \infty$)
- models with bounded state-dependent delay
- models from real applications (computationally challenging)

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Thanks for your attention!