numerical computation of R_0

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calcolo scientifico e modelli matematici
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[3, 4, 5] joint works with

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[3] B., De Reggi, Scarabel, Vermiglio, Wu – Comput. Math. Appl. 2021
[4] B., Florian, Ripoll, Vermiglio – J. Comput. Appl. Math. 2021
[5] B., Kuniya, Ripoll, Vermiglio – J. Sci. Comput. 2020

outline

- historical perspective
- theoretical background
- abstract discretization
- bivariate collocation
- convergence

timeline [7]

- demography: *expected number of newborns*
  - 1886: first ever estimate from fertility table [Böckh]
  - 1925: fully developed concept in demography [Dublin, Lotka]
- epidemiology: *expected number of secondary cases*
  - 1927: celebrated threshold theorem [Kermack, McKendrick]
  - ... incomplete surveys, re-discovering ...
  - 1975: current definition and notation R_0 [Dietz]
  - 1990: full mathematical development [Diekmann, Heesterbeek, Metz]
  - 1991: influential book on infectious diseases [Anderson, May]
- numerics:
  - 2007: rectangles rule [1]
  - 2017: Euler scheme [8]

[1] Bacaër, Guernaoui – J. Math. Biol. 2006
[7] Heesterbeek – Acta Biother. 2002
[8] Kuniya – Appl. Math. Lett. 2017

demography *vs* epidemiology [7]

- demography – each individual of a population of density P produces on average $\mathcal{B}P$ offspring per unit of time for an average of $1/\gamma$ time units:

$$R_0 = \mathcal{B}P \cdot \frac{1}{\gamma}$$

  - $R_0 > 1$ growth, $R_0 < 1$ extinction
- epidemiology – interpretation in terms of critical population density:

$$\frac{\mathcal{B}P}{\gamma} \gtrless 1 \quad \Rightarrow \quad P \gtrless P_c := \frac{\gamma}{\mathcal{B}}$$

[7] Heesterbeek – Acta Biother. 2002

modern account for heterogeneous populations [6]

R_0: expected number of secondary cases produced in a completely susceptible population by a typical infected individual during its entire period of infectiousness

- $\xi \in \Omega$: *structure*, one or more traits characterizing individuals (age, size. . .)
- $S(\xi)$: density of susceptibles in absence of disease
- $A(\tau, \xi, \eta)$: infectivity towards a susceptible with structure ξ of an individual infected τ units of time ago while having structure η
- density of newly infected in S caused by density of infected ϕ

$$(K(S)\phi)(\xi) := S(\xi) \int_\Omega \int_0^\infty A(\tau, \xi, \eta)\, d\tau\, \phi(\eta)\, d\eta$$

next-generation operator

- long run per-generation growth factor:

$$R_0 = \lim_{q\to\infty} \|K(S)^q\|^{1/q}$$

spectral radius $\rho(K(S))$

[6] Diekmann, Heesterbeek, Metz – J. Math. Biol. 1990

unstructured single species [2]

- balance of birth (β) and "death" (μ):

$$x' = \beta x - \mu x \qquad \text{(in } \mathbb{R}\text{)}$$

- asymptotic dynamics ruled by the *malthusian* parameter $\beta - \mu \gtrless 0$
- alternatively, for the birth rate $b(t) := \beta x(t)$, variation of constants gives

$$b(t) = \beta e^{-\mu t} x(0) + \beta \int_0^t e^{-\mu(t-s)} b(s)\, ds$$

- taking $x(0) = 0$, $b \equiv 1$ and $t \to +\infty$ gives R_0 as

$$\beta \int_0^\infty e^{-\mu\sigma}\, d\sigma = \beta \cdot \frac{1}{\mu} \gtrless 1$$

- note that $e^{-\mu t}$
  - is the solution semigroup of $x' = -\mu x$ (absence of birth)
  - gives the survival probability ($= x(t)/x(0)$), hence $1/\mu$ is the life expectancy

[2] Barril, Calsina, Ripoll – Bull. Math. Biol. 2017

structured populations [2]

- let $X = X(\Omega)$ be a Banach lattice of functions $\Omega \subseteq \mathbb{R}^s \to \mathbb{R}$ $(s = 1, 2)$
- *abstract* ODE

$$x' = Bx - Mx \qquad \text{(in } X\text{)}$$

  - birth $B : X \to X$ linear and bounded
  - "death" $M : \mathrm{dom}(M) \subset X \to X$ linear and such that $-M$ generates a C_0-semigroup $\{T(t)\}_{t \geqslant 0}$ with spectral abscissa $s(-M) < 0$
- asymptotic dynamics ruled by the malthusian parameter $s(B - M) \gtrless 0$
- or, equivalently, by the next-generation operator

$$B \int_0^\infty T(\sigma)\, d\sigma = BM^{-1}$$

  through its spectral radius $R_0 = \rho(BM^{-1}) \gtrless 1$
- BM^{-1} is in general linear, bounded and positive

[2] Barril, Calsina, Ripoll – Bull. Math. Biol. 2017

Malthus *vs* R_0

- sign relation [9]:

$$\text{sign}\, s(B - M) = \text{sign}\,[\rho(BM^{-1}) - 1]$$

- pros/cons [2]:
  - rank $(B) \leqslant$ rank $(B - M)$
  - B finite rank: BM^{-1} is compact, whereas $B - M$ is not in general
  - splitting in birth/ "death" not unique $(*)$
- assumption: BM^{-1} compact, implying $R_0 = \rho(BM^{-1}) \geqslant 0$ dominant eigenvalue

[2] Barril, Calsina, Ripoll – Bull. Math. Biol. 2017
[9] Thieme – SIAM J. Appl. Math. 2009
$(*)$ e.g., cell proliferation: $\beta - \mu = 2\beta - (\beta + \mu)$

standard *vs* generalized eigenvalue problems

- $BM^{-1}: X \to X$ is linear, bounded, positive and compact
- yet infinite-dimensional $\Rightarrow$ infinitely-many eigenvalues
- discretize

$$BM^{-1}\psi = \lambda\psi$$

  with a finite-dimensional SEP
- M^{-1} unknown in general, so consider equivalently the GEP

$$B\phi = \lambda M\phi, \quad \phi \in \mathrm{dom}(M)$$

- $\mathrm{dom}(M) \subset X$ more regular than X, plus additional constraints $C\phi = 0$ for some $C : \mathrm{dom}(M) \subset X \to \bar{X}$ with $\bar{X} := X(\bar{\Omega})$ and $\bar{\Omega}$ a boundary of Ω, hence consider

$$\begin{cases} B\phi = \lambda M\phi \\ 0 = \lambda C\phi \end{cases}$$

abstract discretization – 1

- let $X_N \subset X$ be a finite-dimensional approximation space, isomorphous to $\mathbb{R}^N$
- define
  - restriction $R_N : X \to \mathbb{R}^N$
  - prolongation $P_N : \mathbb{R}^N \to X_N$

  such that $R_N P_N = I_N$ (hence $L_N := P_N R_N : X \to X_N$ is a projection)
- act similarly for $\bar{N} < N$ on
  - $\bar{X}$ with $\bar{X}_{\bar{N}}$, $\bar{R}_{\bar{N}}$, $\bar{P}_{\bar{N}}$ and $\bar{L}_{\bar{N}}$
  - $X^\circ := X(\Omega \setminus \bar{\Omega})$ with $X^\circ_{N-\bar{N}}$, $R^\circ_{N-\bar{N}}$, $P^\circ_{N-\bar{N}}$ and $L^\circ_{N-\bar{N}}$

abstract discretization – 2

- discretize

$$\begin{cases} B\phi = \lambda M\phi \\ 0 = \lambda C\phi \end{cases} \qquad \text{(in } X\text{)}$$

with

$$B_N\Phi = \lambda M_N\Phi \qquad \text{(in } \mathbb{R}^N\text{)}$$

for

$$B_N := \begin{pmatrix} R^{\circ}_{N-\bar{N}} BP_N \\ 0_{\bar{N},N} \end{pmatrix}, \quad M_N := \begin{pmatrix} R^{\circ}_{N-\bar{N}} MP_N \\ \bar{R}_{\bar{N}} CP_N \end{pmatrix}$$

- examples:
  - pseudospectral collocation in L^1
  - Fourier expansion in L^2

age-immunity model [3]

- individuals characterized by age $a \in [0, \bar{a}]$ and immunity level $w \in [0, 1]$ waning as $w' = -g(w)$ for some positive g
- susceptibles $s = s(t, a, w)$ and infected $i = i(t, a, w)$ at time t, age a and immunity w ruled by

$$\begin{cases} \partial_t s + \partial_a s - \partial_w [g(w)s] = -[\mu(a) + \lambda(i, w) + \eta(i, w)]s \\ \partial_t i + \partial_a i = \lambda(i, w)s - [\mu(a) + \gamma]i \\ g(1)s(t, a, 1) = \gamma \int_0^1 i \, dw + \int_0^1 \eta(i, w) s \, dw, \quad i(t, a, 1) = 0 \\ s(t, 0, w) = \mathcal{B}(w), \quad i(t, 0, w) = 0 \end{cases}$$

with

- force of infection $\lambda(i, w) := \beta(w)p(i)$
- force of boosting $\eta(i, w) := [1 - \beta(w)]p(i)$
- probability $\beta(w)$ of infection upon contact
- infection pressure $p(i) := \int_0^1 \nu(\omega) \int_0^{\bar{a}} i(t, a, \omega) \, da \, d\omega$ (infectivity ν)

[3] B., De Reggi, Scarabel, Vermiglio, Wu – Comput. Math. Appl. 2021

linearization, B and M

- disease-free equilibrium $\bar{s}(a, w) > 0$, $\bar{i}(a, w) = 0$ by integration along characteristics
- the linearized equation for the infected reads

$$\begin{cases} \partial_t x + \partial_a x = \lambda(x, w)\bar{s}(a, w) - [\mu(a) + \gamma]x \\ x(t, a, 1) = 0 \\ x(t, 0, w) = 0 \end{cases} \qquad (\text{in } \mathbb{R})$$

- equivalently,

$$x' = Bx - Mx \qquad (\text{in } X := L^1([0, \bar{a}] \times [0, 1]))$$

for

- $x(t) : (a, w) \mapsto x(t, a, w)$
- $(B\phi)(a, w) := \beta(w) \left(\int_0^1 \nu(\omega) \int_0^{\bar{a}} \phi(\xi, \omega)\, d\xi\, d\omega \right) \bar{s}(a, w)$
- $(M\phi)(a, w) := \partial_a \phi(a, w) + [\mu(a) + \gamma]\phi(a, w)$
- $\mathrm{dom}(M) := \{\phi \in X \;:\; \partial_a \phi \in X \text{ and } \phi(0, w) = \phi(a, 1) = 0\}$

tensorial bivariate collocation

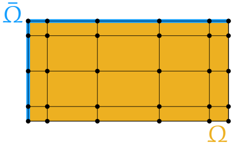
- recall:

$$\begin{cases} B\phi = \lambda M\phi \\ 0 = \lambda C\phi \end{cases} \quad \text{in } X = L^1([0,\bar{a}]\times[0,1]) \text{ discretized by } \; B_N\Phi = \lambda M_N\Phi \; \text{ in } \mathbb{R}^N$$

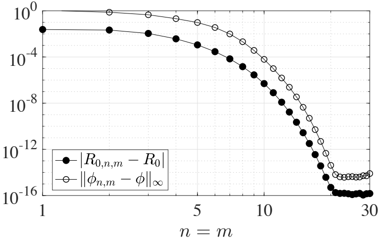
with

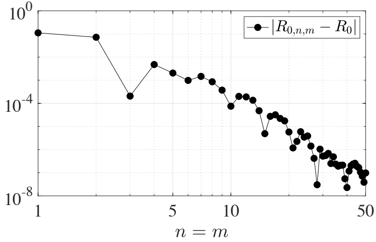
$$B_N := \begin{pmatrix} R^{\circ}_{N-\bar{N}} B P_N \\ 0_{\bar{N},N} \end{pmatrix}, \quad M_N := \begin{pmatrix} R^{\circ}_{N-\bar{N}} M P_N \\ \bar{R}_{\bar{N}} C P_N \end{pmatrix}$$

- concretely:
  - $[0,\bar{a}]$ discretized by $0 =: a_0 < a_1 < \cdots < a_n := \bar{a}$
  - $[0,1]$ discretized by $0 =: w_0 < w_1 < \cdots < w_m := 1$
  - $\Phi = \mathrm{vec}(\Phi_{i,j})_{i=0,\dots,n,j=0,\dots,m}$
  - $P_N\Phi = \phi_{n,m}$ bivariate polynomial interpolant
  - $R^{\circ}_{N-\bar{N}}$: evaluation at grid points $(a_i,w_j)_{i=1,\dots,n,j=0,\dots,m-1}$
  - $\bar{R}_{\bar{N}}$: evaluation at grid points $(a_0,w_j)_{j=0,\dots,m}$ and $(a_i,w_m)_{i=1,\dots,n}$
  - $N=(n+1)(m+1)$, $\bar{N}=n+m+1$



results





$g(w) = \beta(w) = \nu(w) = 1 - w$
$\mathcal{B}(w) = (1 - w)^2$
$\mu \equiv \gamma = 1,\ \bar{a} = 2$

R_0 and ϕ known exactly
$\bar{s}$ analytic

$g(w) = w,\ \beta(w) = \nu(w) = 1 - w$
$\mathcal{B}(w) = (1 - w)^2$
$\mu(a) = 1/(\bar{a} - a)^2,\ \gamma = 1,\ \bar{a} = 2$

R_0 and ϕ unknown
$\bar{s}$ only C^1

convergence: one structure, $\Omega \subset \mathbb{R}$ [5]

$$\|\phi_N - \phi\|_X = \begin{cases} O(N^{-s} \log N) & \text{for coefficients of class } C^s \\ O(k^{-N} \log N), \ k > 1 & \text{for analytic coefficients} \end{cases}$$

$$|\lambda_N - \lambda| = O(\|\phi_N - \phi\|_X^{1/\alpha}), \quad \alpha \text{ algebraic multiplicity of } \lambda$$

- steps of the proof:
  - the eigenvalue problem leads basically to an ODE or to a Volterra integro-differential equation
  - bound the relevant collocation error $\|\phi_N - \phi\|_X$
  - consolidated tools as variation of constants or resolvent theory leads to a characteristic equation for the eigenvalues
  - compare with the discrete version from collocation and apply Rouché's Theorem to bound $|\lambda_N - \lambda|$

[5] B., Kuniya, Ripoll, Vermiglio – J. Sci. Comput. 2020

convergence: two structures, $\Omega \subset \mathbb{R}^2$

- work in progress
- apparently no trivial extension from $\Omega \subset \mathbb{R}$:
  - the eigenvalue problem leads to a PDE
  - no easy tool to get a characteristic equation
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- promising alternative through an abstract approach:

(SEP)

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$\downarrow$

$$\boxed{\begin{pmatrix} R^{\circ}_{N-\bar{N}} B P_N \\ 0_{\bar{N},N} \end{pmatrix} \Phi = \lambda \begin{pmatrix} R^{\circ}_{N-\bar{N}} M P_N \\ \bar{R}_{\bar{N}} C P_N \end{pmatrix} \Phi}$$

(GEP$_N$)

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$$\Big\uparrow{\scriptstyle N,\bar{N},N-\bar{N}\to\infty}$$

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\begin{tikzcd}
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\underset{(\text{SEP}_{N-\bar{N}})}{\boxed{R^{\circ}_{N-\bar{N}} B M^{-1} P^{\circ}_{N-\bar{N}} \Psi = \lambda \Psi}} \arrow[u, "{N,\bar{N},N-\bar{N} \to \infty}"] \arrow[r, leftrightarrow] & \underset{(\text{GEP}_N)}{\boxed{\begin{pmatrix} R^{\circ}_{N-\bar{N}} B P_N \\ 0_{\bar{N},N} \end{pmatrix} \Phi = \lambda \begin{pmatrix} R^{\circ}_{N-\bar{N}} M P_N \\ \bar{R}_{\bar{N}} C P_N \end{pmatrix} \Phi}}
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\end{tikzcd}
$$

so far

- M does not regularize, whereas M^{-1} does
- let σ^* denotes nontrivial eigenvalues, with multiplicities and relevant eigenvectors
- if $BM^{-1}X \subseteq Y \subset X$ and $\|L^\circ_{N-\bar{N}} - I_X\|_{X \leftarrow Y} \to 0$ as $N, \bar{N}, N - \bar{N} \to \infty$, then

$$\lim_{N,\bar{N},N-\bar{N}\to\infty} \sigma^*(\mathrm{SEP}_{N-\bar{N}}) = \sigma^*(\mathrm{SEP})$$

- the following standard property seems crucial to understand the relation between $\sigma^*(\mathrm{SEP}_{N-\bar{N}})$ and $\sigma^*(\mathrm{GEP}_N)$:

$$\|(\lambda I_d - A)^{-1}\| \geqslant \frac{1}{\mathrm{dist}(\lambda, \sigma(A))}, \quad \lambda \notin \sigma(A), \quad A \in \mathbb{R}^{d\times d}$$

  - need for careful extensions to pencils $\lambda B - A : U \to V$ (possibly with $\dim U < \dim V \leqslant \infty$ or vice versa)

open

- abstract convergence proof (linear operator pencils)
- lack of compactness
- more structures (Padua points)
- user-friendly tool (codes @ `http://cdlab.uniud.it/software`)

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thank you all for the attention

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